# TO COMPARE THE DOSIMETRY OF THREE- LINEAR ACCELERATOR BASED STEREOTACTIC RADIOTHERAPY (SRT) TECHNIQUES STATIC CONFORMAL FIELD (SCF), STATIC CONFORMAL ARC (SCA) AND DYNAMIC CONFORMAL ARC (DCA) FOR PITUITARY ADENOMA AND CRANIOPHARYNGIOMA

***Dissertation Submitted In Partial Fulfilment Of***

**MD BRANCH IX RADIOTHERAPY**

**EXAMINATION APRIL 2016**

**To**

**THE TAMILNADU Dr. M.G.R MEDICAL UNIVERSITY**

**CHENNAI – 600032**

By,

**Dr. MUTTANAGOUDA GIRIYAPPAGOUDAR**
**Post Graduate Registrar**
**Department Of Radiotherapy (Branch IX)**
**Christian Medical College**
**VELLORE-632002, Tamilnadu, India**

**April 2016**

# Certificate

I Muttanagouda Giriyappagoudar, a Post Graduate Registrar in the department of Radiotherapy, Christian Medical College, hereby declare that the dissertation entitled **"TO COMPARE THE DOSIMETRY OF THREE- LINEAR ACCELERATOR BASED STEREOTACTIC RADIOTHERAPY (SRT) TECHNIQUES STATIC CONFORMAL FIELD (SCF), STATIC CONFORMAL ARC (SCA) AND DYNAMIC CONFORMAL ARC (DCA) FOR PITUITARY ADENOMA AND CRANIOPHARYNGIOMA."** is a bonafide work done by me. This is being submitted to The Tamil Nadu Dr. M. G. R Medical University in partial fulfilment of the MD Radiotherapy (Branch IX) examination conducted in April 2016.

Dr. MUTTANAGOUDA GIRIYAPPAGOUDAR
POST GRADUATE REGISTRAR
DEPARTMENT OF RADIOTHERAPY
CHRISTIAN MEDICAL COLLEGE
VELLORE-632002


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This is to certify that the dissertation entitled **"TO COMPARE THE DOSIMETRY OF THREE- LINEAR ACCELERATOR BASED STEREOTACTIC RADIOTHERAPY (SRT) TECHNIQUES STATIC CONFORMAL FIELD (SCF), STATIC CONFORMAL ARC (SCA) AND DYNAMIC CONFORMAL ARC (DCA) FOR PITUITARY ADENOMA AND CRANIOPHARYNGIOMA."** is a bonafide work done by Dr.Muttanagouda Giriyappgoudar, Post Graduate Registrar in the Department of Radiotherapy, Christian Medical College, Vellore during the period from June 2014 to September 2015 and is being submitted to The Tamil Nadu Dr. M. G. R Medical University in partial fulfilment of the MD Branch IX Radiotherapy examination conducted in April 2016.

Research Guide
Dr. SELVAMANI B
Professor dept of Radiotherapy
Christian Medical College
Vellore, India-632002


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Department of Radiotherapy
Christian Medical College
Vellore, India-632002

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Vellore, India-632002

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PG Registrar
Department of Radiotherapy
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Dear Dr. Muttanagouda Giriyappagoudar,

I enclose the following documents:-

1. Institutional Review Board approval 2. Agreement

Could you please sign the agreement and send it to Dr. Nihal Thomas, Addl. Vice Principal (Research), so that the grant money can be released.

With best wishes,

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The Committees reviewed the following documents:

1. IRB Application format
2. Curriculum Vitae' of Drs. Muttanagouda Giriyappagoudar, Selvamani. B, Sunitha Susan Varghese, I. Rabi Raja Singh, Mr. A Sivasakthi, Ms. Reka. K
3. Letter requesting for ICF Waiver
4. Proforma
5. No of documents 1 – 4

The following Institutional Review Board (Blue, Research & Ethics Committee) members were present at the meeting held on January 12th 2015 in the CREST/SACN Conference Room, Christian Medical College, Bagayam, Vellore 632002.



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Tel : 0416 - 2284294, 2284202 Fax : 0416 - 2262788, 2284481 E-mail : research@cmcvellore.ac.in

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We approve the project to be conducted as presented.

The Institutional Ethics Committee expects to be informed about the progress of the project, any **adverse events** occurring in the course of the project, any **amendments in the protocol and the patient information / informed consent**. On completion of the study you are expected to submit a copy of the **final report**. Respective forms can be downloaded from the following link: http://172.16.11.136/Research/IRB_Polices.html in the CMC Intranet and in the CMC website link address: http://www.cmch-vellore.edu/static/research/Index.html.

*Fluid Grant Allocation:*

*A sum of 3,000/- INR (Rupees Three Thousand only) will be granted for 8 months.*

Yours sincerely

Dr. Alfred Job Daniel
Chairperson, Research Committee & Principal
Institutional Review Board
Christian Medical College, Vellore

Chairperson (Research Committee) &
Principal
Christian Medical College
Vellore - 632 002, Tamil Nadu, India

Cc: Dr. Selvamani. B, Radiotherapy, CMC, Vellore.

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Ethics Committee Blue, Office of Research, 1st Floor, Carman Block, Christian Medical College, Vellore, Tamil Nadu 632 002.
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DEPARTMENT OF RADIOTHERAPY

CHRISTIAN MEDICAL COLLEGE

VELLORE 632004

*DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT OF*

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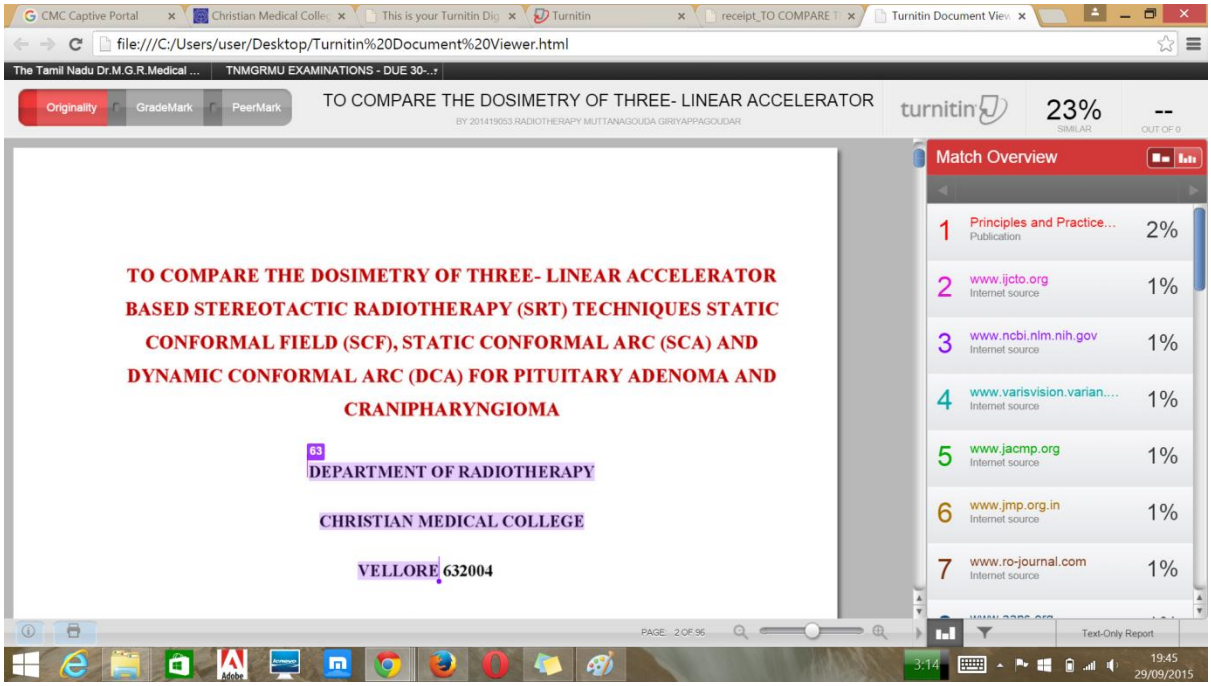
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# Contents

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# Abbreviations

| | |
|---|---|
| **Sv** | **Seivert** |
| **3DCRT** | Three Dimesnsional Conformal Radiotherapy |
| **4 MV** | 4 Megavoltage |
| **ANOVA** | Analysis of Variance |
| **BEV** | Beam's Eye View |
| **BRW** | Brown-Robert-Wells |
| **SCA** | Static Conformal Arc |
| **SCF** | Static conformal field |
| **cGy** | Centi Gray |
| **CI** | Conformity Index |
| **LINAC** | Linear accelerator |
| **CNS** | central nervous system |
| **CT** | Computed Tomography |
| **DCA** | Dynamic Conformal Arc |
| **dDVH** | Differential dose volume histogram |
| **DVHs** | dose-volume histograms |
| **EUD** | Equivalent uniform dose |
| **GTC** | Gill-Thomas- Cosman |
| **GTV** | Gross Tumour Volume |
| **Gy** | Gray |
| **HI** | Homogeneity Index |
| **ICRU** | International commission on radiological units |
| **iDVH** | Integral Dose volume histogram |
| **IGRT** | image guided radiotherapy |
| **IMRT** | Intensity Modulated Radiotherapy |
| **IQ** | Intelligence Quotient |
| **LCMA** | Linac Couch Mount Assembly |
| **LTLF** | Linac Target Locator Frame |
| **mMLC** | micro Multileaf Collimators |

| | |
|---|---|
| **MRI** | Magnetic Resonance Image |
| **MU** | Monitory Units |
| **MV** | Megavoltage |
| **NTCP** | normal tissue complication probability |
| **OARs** | organs at risk |
| **PTV** | planning target volume |
| **QUANTEC** | Quantitative Analyses of Normal Tissue Effects in the Clinic |
| **RHO** | Spearman rank correlation |
| **RI** | reference isodose |
| **RIV** | Reference isodose volume |
| **RTOG** | Radiation Therapy Oncology Group |
| **SBRT** | Stereotactic body radiotherapy |
| **SCA** | Static Conformal Arc |
| **SCF** | Static Conformal Field |
| **SD** | Standard Deviation |
| **SRS** | Stereotactic Radiosurgery |
| **SRT** | Stereotactic radiotherapy |
| **T1W** | T1 Weighted |
| **T2W** | T2 Weighted |
| **TCP** | Tumour control probability |
| **TPS** | Treatment Planning System |
| **TV** | Target Volume |

## ABSTRACT

**Title**: To compare the dosimetry of three- linear accelerator based stereotactic radiotherapy (SRT) techniques Static Conformal Field (SCF), Static Conformal Arc (SCA) and Dynamic Conformal Arc (DCA) for Pituitary adenoma and Cranipharyngioma.

**Aim**: To compare the dosimetric outcomes of the three linear accelerator based stereotactic radiotherapy techniques, Static Conformal Field (SCF), Static conformal Arc and Dynamic conformal arc (DCA), for the treatment of Pituitary adenoma and Craniopharyngioma.

**Materials and methods:** Computer image sets of 20 patients who have been diagnosed either as Pituitary adenoma or Craniopharyngioma and treated with Stereotactic radiotherapy (SRT) were selected for the study. For each data set, three SRT plans, one each with SCF, SCA and DCA techniques were generated using Brain LAB, iPlan RT V.4.5.3, TPS software. The Conformity index (CI), Homogeneity index (HI), Quality of coverage of the target, Dose volume histograms for the target and organs at risk and the time taken to deliver treatment were compared across these three sets of plan.

**Results**: There were 12 patients with Pituitary adenoma and eight patients with Craniopharyngioma. All patients had surgical excision of the tumour prior to radiotherapy. The conformity and homogeneity indices were comparable across three techniques. The quality of coverage was comparable in static conformal field and DCA techniques, where as it is slightly inferior in static conformal arc technique. The organs at risk are better spared in SCF and DCA techniques compared to SCA technique. The time taken to deliver treatment was lesser in SCF compared to SCA and DCA.

**Conclusions**: The Conformity Index and Homogeneity Index were comparable across the three plans but Quality of target coverage was superior in DCA. Dynamic Conformal Arc (DCA) technique was the best technique among the three in achieving all the indices. Doses to normal organs, Optic Chiasm and Brain stem were better controlled in SCF technique than SCA and DCA technique.

# 1 AIMS

To compare the dosimetry of three- linear accelerator based stereotactic radiotherapy (SRT) techniques Static Conformal Field (SCF), Static Conformal Arc (SCA) and Dynamic Conformal Arc (DCA) for Pituitary adenoma and Craniopharyngioma.

## 2 OBJECTIVES

### 2.1 Primary Objectives:

a) Dosimetric comparison of three stereotactic radiotherapy treatment techniques Static Conformal Field (SCF), Static Conformal Arc (SCA) and Dynamic Conformal Arc (DCA) for Pituitary adenoma and Craniopharyngioma.

b) To compare the dosimetric analysis performed using DVH's and 2D dose displays, RTOG Quality Assurance guidelines of SRT using Conformity Index (CI), Homogeneity Index (HI) and Quality of target coverage of the three techniques. Analysis of the plans was also performed using parameters like maximum dose, minimum dose and mean dose.

### 2.2 Secondary Objectives:

a) To assess the east of treatment planning, time required for delivering treatment and analysing the number of monitor units required to deliver intended treatment of the three Linear Accelerator based Stereotactic Radiotherapy (SRT) techniques.

b) To understand the efficacy of three Linear Accelerator based Stereotactic Radiotherapy (SRT) techniques in reducing the dose of radiation to the brain.

## 3 HYPOTHESIS

Linear accelerator based, Dynamic Conformal Arc (DCA) stereotactic radiotherapy is a better technique with improved homogeneity, conformity indices and better sparing of organs at risk for the treatment of Pituitary adenoma and Craniopharyngioma.

# INTRODUCTION

# 4 INTRODUCTION

Stereotactic Radiotherapy is highly précised conformal radiation therapy technique. The word stereotaxic or stereotactic is composed of the Greek word “stereos” meaning three dimensional and the Latin word “tactus” which means to touch(1). Stereotactic approach is used to locate the target with help of three dimensional coordinate system located deep within the body especially in the brain. Stereotactic method of radiation delivery evolved from an investigational concept in animals into a main stream neurosurgical procedure for the management of a wide variety of brain disorders (2).

Stereotactic Radiosurgery was started with Gamma Knife, which was discovered by the Lars Leksell. Later the Linear Accelerator based Stereotactic Radiotherapy techniques like arc therapy and static conformal therapy were developed. Invention of the micro Multileaf Collimators (mMLC), development of newer treatment planning system software and advances in imaging techniques lead to delivery of highly précised conformal radiotherapy. This technique of stereotactic delivery of radiation uses a special immobilisation device along with three-dimensional coordinate system to locate and deliver radiation. In the case of SRS all of the radiation is delivered in a single fraction where as stereotactic radiotherapy uses multiple standard fractionation schedules, which has radiobiological advantage of recovery from radiation damage for surrounding normal tissues. Fractionated stereotactic radiotherapy (SRT) has an additional advantage of irradiation of the larger tumours and tumours that are located closely to the eloquent areas of the brain such as optic apparatus. SRT has been reported as safe and effective in treating Pituitary adenoma and Craniopharyngiomas. Various techniques of delivering SRT have been defined in the literature(3–7). Non

coplanar Static Conformal Field (SCF), Static Conformal Arc (SCA) and Dynamic Conformal Arc (DCA) radiotherapy are the three methods of Linear Accelerator based SRT techniques. In SCA therapy, shape of the field aperture remains constant during an arc. In DCA the shape of the micro MLC is automatically adjusted to the projected shape of the target in beams eye view for every 10 degree increment from the gantry start angle till the end. The SCF plan consists of six to ten non-coplanar static fields; each field is individually shaped to the beams eye view projection of the target using microMLC.

Dynamic Conformal arc technique is an efficient technique in delivering highly conformal and homogenous dose which also reduces the dose to surrounding normal structures in intracranial sellar and suprasellar tumours like meningiomas, pituitary adenoma and craniopharyngiomas(8).

The incidence of the sellar tumours accounts for 0.73 per 100,000 person years(9). Sellar tumours mainly include Pituitary adenomas and Craniopharyngiomas. Tumors of the pituitary gland and sellar region represent approximately 10-15% of all brain tumors, of which pituitary adenomas are the most common(10,11). Pituitary gland is located in the sella turcica (hypophyseal fossa) which is a part of the sphenoid bone. Pituitary gland is related above to optic chiasm; patients with Pituitary adenomas can present with visual disturbances because of the pressure effect on the optic pathway. Craniopharyngiomas are the third most common intracranial tumour in children after gliomas and medulloblastomas(12). They account for 5 to 10 percent of all childhood brain tumours. These are solid or mixed solid-cystic benign tumours that arise from

remnants of Rathke's pouch. Pituitary adenoma and Craniopharyngiomas are in close proximity to the optic chiasm, tracts and brain stem.

Medical intervention may reduce the size of the tumour of secreting Pituitary adenoma and decrease the function. Surgery normalises the hormonal levels quickly and relieves the pressure symptoms. Radiation therapy is reserved for the patient's with residual disease after the surgery or when the tumour recurs after surgery. Radiation is also indicated in patients who are not candidates for surgical excision due to co morbidities. The recommended radiation dose for non-functioning pituitary adenoma, functioning pituitary adenoma and craniopharyngiomas are 4500cGy, 5040cGy and 5400cGy respectively in conventional fractionation(13,14). Normalisation of the hormonal levels can take months to years after the radiation therapy.

Radiation therapy is effective in controlling the tumour growth in as high as 90-100% in many series regardless of the type of adenoma and technique of radiation used. The toxicities related to the radiation are generally low(15). The various modalities of delivering radiation include two dimensional external beam radiation therapy, conformal radiation therapy (3DCRT), Radiosurgery (SRS), Stereotactic radiation therapy (SRT) or Proton beam radiation therapy. Since adenomas are mostly small, radiologically well circumscribed and anatomically closely related to the optic apparatus, these tumours attracted the use of stereotactically guided high precision radiotherapy. More recently many reports indicated promising outcomes with SRT (16). In SRT patients are immobilised with a relocatable stereotactic Gill-Thomas-Cosman (GTC) frame and tumor localization is achieved through CT scanning using a

Brown-Robert-Wells (BRW) localisation system. There are three different types of LINAC based SRT techniques defined in the literature.(3,17,18)

Although data for qualitative of stereotactic techniques are available for skull base meningioma, optic pathway gliomas, similar comparison for the three plans for Pituitary adenoma and Craniopharyngioma are lacking. Moreover in these tumours the optic chiasm is almost lying very close or sometime it is abutted by the tumour. These tumours are also in close contact with brain stem posteriorly. These are some of the features of these tumours which necessitate highly conformed homogenous dose distribution in the target so as to avoid normal structures. Patients with Pituitary adenoma and Craniopharyngioma have excellent long term survival advantage, so these patients are likely to benefit from high precision radiotherapy as it may reduce the risk of developing late side effects.

In our study a qualitative and a quantitative dosimetric analysis of the three conventional SRT techniques are compared with respect to indices of conformity and homogeneity, quality of coverage as proposed by RTOG and also dose to normal tissues with the help of dose volume histograms. In this study we also analysed the volume of the brain getting low dose of radiation, 5Gy in these three techniques and also doses such as 6Gy, 10Gy, 20Gy and 40Gy.

In the centres, where the patient load is high, every effort has to be made to reduce the time consumption for planning and treatment delivery. In this regard additional comparison of the techniques is made in terms of ease of planning, number of monitor units required to deliver a prescribed dose of radiation and time taken to deliver the prescribed dose.

# REVIEW OF LITERATURE

# 5 REVIEW OF LITERATURE

## 5.1 Introduction to stereotactic radiotherapy

### 5.1.1 Stereotaxy

The word stereotaxic or stereotactic is composed of the Greek word “stereos” meaning three dimensional and the Latin word “tactus” which means to touch(1). Stereotactic approach is used to locate the target with help of three dimensional coordinate system located deep within the body especially in the brain. The different terms are being used for the different actions performed using stereotactic methods. For example biopsy of a lesion in the brain using stereotactic approach is known as stereotactic biopsy. Radiation delivery to the tumour using stereotactic method is known as Stereotactic Radiosurgery or Stereotactic Radiotherapy.

Stereotactic Radiosurgery (SRS) and Stereotactic Radiotherapy (SRT) are types of external beam radiotherapy techniques to administer precisely directed, high-dose ionising radiation that conforms to an intracranial target to create a desired radiobiologic response while minimizing radiation dose to surrounding normal tissues(19). In stereotactic radiosurgery (SRS), radiation is delivered in a single fraction, where as in stereotactic radiotherapy (SRT), radiation is administered in multiple small fractions.

Stereotactic radiotherapy involves daily application of a non-invasive guiding device for the purpose of immobilisation(20). The stereotactic irradiation is performed in an attempt to reduce the dose of radiation to the surrounding normal tissue over

conventional radiation therapy and also to provide greater dose homogeneity to the target tissue.

### 5.1.2 Stereotactic Radiosurgery versus Stereotactic Radiotherapy

Both SRS and SRT are effective as an adjuvant or as a primary treatment for many intracranial tumours(21). Both modalities are slightly different technically, but the principles remain same. Both modalities are used in different clinical scenarios but provide safer treatment options for patients with intracranial lesions. SRS alone may not be suitable in all the cases, the limitations are related to many factors like tumour size and proximity to eloquent structures especially the optic apparatus (22,23). Many authors have reported better clinical outcomes using SRS for meningioma smaller than 3cm in size or 20ml in volume with adequate distance of about 2-4 cm from optic apparatus(24–26). Intracranial tumours encasing or compressing eloquent structures such as the optic apparatus, cranial nerves and brain stem treated with SRT will benefit from the radiobiological advantages of fractionation (27).

With advent of stereotactic radiotherapy it is possible to treat large intracranial tumours up to about 4cm such as incompletely resected tumours and also in situations where the risk of resection carries high morbidity and mortality. SRS is not indicated in tumours larger than 4 cm, since adequate coverage could not be achieved without limiting the toxicity(28). SRT is a treatment option that can be used when the risk of SRS is high in case of tumours involving brain stem, optic pathways(29,30). Andrews, et al. in a study investigating the safety and efficacy of stereotactic radiotherapy as an

alternative therapy to surgical resection for optic nerve sheath meningiomas, demonstrated preservation of the vision in 92% of the patients and there was an improvement of the vision in 42% of the patients (31). The safety of SRT has been established in the treatment of optic nerve sheath meningiomas.

Rationale for using SRT is primarily to reduce the radiation damage to the surrounding structures and to obtain homogenous dose distribution. Though the concepts and outcomes of stereotactic radiosurgery and radiotherapy are similar in certain indications but the radiobiology of the both approaches is fundamentally different(32). In SRS, radiation therapy leads to ischemia and perfusion injury because of the endothelial apoptosis, resulting in cell death. Whereas fractionated radiotherapy relies on a different sensitivity of the target and the surrounding normal tissue to the total accumulated radiation dose (33)..

### 5.1.3 Advantages of fractionated stereotactic radiotherapy

Selection of the patients for SRT differs from that of SRS, as SRT has an advantage over SRS in case of tumours located very close to (<3-5mm) eloquent normal structures like optic nerves and chiasm as the tolerance of these structures may not permit delivery of high dose single fractionated radiation. The tolerance of these organs is limited to 8-10Gy in single fraction (30). And also SRS may not be the treatment of choice for bigger tumours having diameter of more than 4cm due to high dose of radiation that passes through large areas of normal structures (34).

With radiosurgery, the risk of developing Radiation Induced Optic Neuritis is estimated to be 0-2% if the optic apparatus is constrained to 10Gy(30). However, when the dose to the optic apparatus exceeds 12Gy, the risk rises rapidly and is 78% with doses ≥ 15Gy(30). The time interval between the fractions in SRT enables normal tissues to repair thorough four Rs' of Radiobiology - Reoxygenation, Reassortment, Repopulation and Repair improves the treatment outcome as a consequence of radiobiological effect(35).

## 5.2 Techniques stereotactic radiotherapy

The technique of stereotactic radiotherapy uses the same principle as SRS in terms of beam shaping, use of micro multileaf collimator (mMLC), rotation of the gantry etc. The description of the evolution of radiosurgery applies to stereotactic radiotherapy as well.

The concept of radiosurgery was introduced 4 decades ago by Lars Leksell. He proposed the technique of focussing multiple nonparallel beams of external beam radiation on an intracranial target, resulting in high dose of radiation to the target and low dose of radiation to the surrounding structures. He developed Gamma knife which uses 201 Cobalt sources.

An alternate radiosurgical solution, LINAC Radiosurgery was first adapted by Betti and Derechinsky in 1984 (36). In 1985, Colombo, *et al.*,(3) described such a system and LINACs have subsequently been modified in various ways to achieve the precision and accuracy required for radiosurgical applications(37). In 1986, first

system of LINAC based Stereotactic radiation technique was developed in University of Florida(38). Then LINAC based stereotactic technique became popular in multiple centres around the world as other treatments also possible with LINAC compared to Gamma Knife which is dedicated only for Stereotactic treatments.

"Novalis Tx" is another commercially available technological advancement in delivering high precision stereotactic radiosurgery using Linear Accelerator(39). Novalis Tx uses robotically controlled treatment table and performs radiosurgery in a frameless mode, which avoids discomfort to the patient as it does not require the surgical placement of the frame. This technique is used for treatment of both intracranial and extracranial tumours. This program is designed to supplement conventional linear accelerators with advanced beam shaping technology and image-guidance tool to deliver high precision radiation.

### 5.3 LINAC based stereotactic radiotherapy

LINAC based Radiosurgery technique used several collimated coplanar or non-coplanar radiation beams on a stereotactically focussed target (3). So the multiple static beams or arcs, in co-planar or non-coplanar beams that converge on the target volume are used.

LINAC based stereotactic radiotherapy or radiosurgery is either a modification of a conventional LINAC for the purpose of SRT or LINAC that is specifically designed for the stereotactic purpose. LINAC has got primary and secondary collimators located in the head of the gantry. Additional collimators are fitted to the beam head

when it is used for the SRT procedure. This system uses either narrow circular cones (collimators) of different size or micro multileaf collimator (mMLC) (Fig 1) to shape the treatment fields(40). The one with mMLC comprises computer controlled multiple motorized tungsten leafs, (micro multileaf collimators-mMLC) which are suited for shaping specific fields of therapeutic intent both in a static fashion as well as dynamically via leaf-movement during the treatment. This mMLC is commercially available in different thickness from 2.5mm to 5mm.

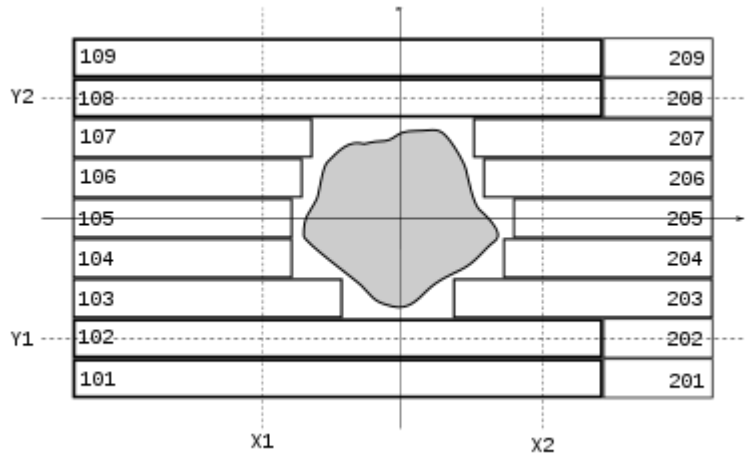



**Fig 1: Micro multileaf collimators (mMLC) shaping the field to the target(40)**

The combination of gantry and couch rotation around the patient results in a variety of different techniques for beam delivery and the advent of mMLC resulted in dynamic beam shaping, in which these MLC take the shape of the tumour in beam's eye view while the gantry moves from one position to the other.

"True beam" is a commercially available technology developed by Varian Medical System, which is integrated, Linear accelerator based technique, which dynamically synchronises imaging, motion management and positioning and treatment of the

patient. This technique is used for all forms of advanced radiation therapy like image guided radiotherapy (IGRT), SRS, Intensity Modulated Radiotherapy (IMRT) and Stereotactic body radiotherapy (SBRT).

SRT techniques require three-dimensional imaging and localization techniques that determine the exact coordinates of the target within the body. SRT requires rigid immobilisation system to immobilise and carefully position the patient. This immobilisation technique is reproduced every day for and throughout the period of treatment.

### 5.4 Indications for SRS and SRT:

Stereotactic radiosurgery or radiotherapy are indicated in many intracranial disorders as mentioned below(41)

- **Functional disorders**
  - Trigeminal neuralgia
  - Vascular malformation
  - Arteriovenous malformation
  - Cavernous malformation
- **Benign tumours**
  - Meningioma
  - Pituitary adenoma
  - Craniopharyngioma
  - Vestibular schwannoma

Trigeminal schwannoma

Jugular foramen schwannoma

Glomus tumor

- **Metastases (less than four in number)**
- **Skull base tumors** (42)**.**

Chordoma

Chondrosarcoma

## 5.5 Clinical indications of SRT

Fractionated stereotactic radiotherapy is also used for most of the above mentioned brain tumours including benign and malignant tumours. The choice of fractionated stereotactic radiotherapy depends on the clinical scenario, location of the tumour and relationship with the neighbouring structures and clinical or therapeutic intention and the sensitivity of the surrounding normal organ at risk. Tumours that are less than 5cm and closer to the optic chiasm (2-4 cm)and brainstem, or the tumours that encase the optic chiasms, cranial nerves or brainstem are not treated with SRS instead these tumours are ideal for treatment with SRT, (22,23). Safety and efficacy of SRT has been established in the case of optic nerve sheath tumours, meningiomas and other skull based tumours including pituitary adenoma and craniopharyngioma. SRT delivers radiation more homogenously with better conformity so the tumours that benefit from more homogenous distribution will be treated with SRT. This will benefit especially in skull base tumours to avoid functional morbidities (21).

## 5.6 Immobilisation system for stereotactic radiotherapy

Primary objective of radiation therapy involves accurate delivery of the prescribed dose of radiation to the target while sparing the surrounding critical normal structures. Positioning errors may lead to inaccurate dose delivery resulting in unexpected outcome. Geometric accuracy of radiotherapy depends on ability of positioning system to reproduce same geometrical position beginning from CT simulation to the completion of the treatment.

Variety of commercially available immobilisation devices are reported in the literature. For stereotactic radiotherapy, relocatable Gill-Thomas-Cosman (GTC) head frame is used, which is a non invasive localization and immobilisation technique providing accuracy of patient repositioning on the order of 1 mm (43). GTC frame uses the dental impression of the patient's upper teeth (dental appliance) anteriorly, a headrest with an individualized occipital pad posteriorly and adjustable straps (20). GTC frame is fixed to the patient's head and then rigidly to the CT scanner couch rigidly. The Brown-Roberts-Wells (BRW) localiser frame (Fig 2) is clamped to the GTC frame. The BRW coordinate system is specified by images of nine localization rods (Fig 3, 4) on CT slices. The CT images were then transported to the treatment planning system.

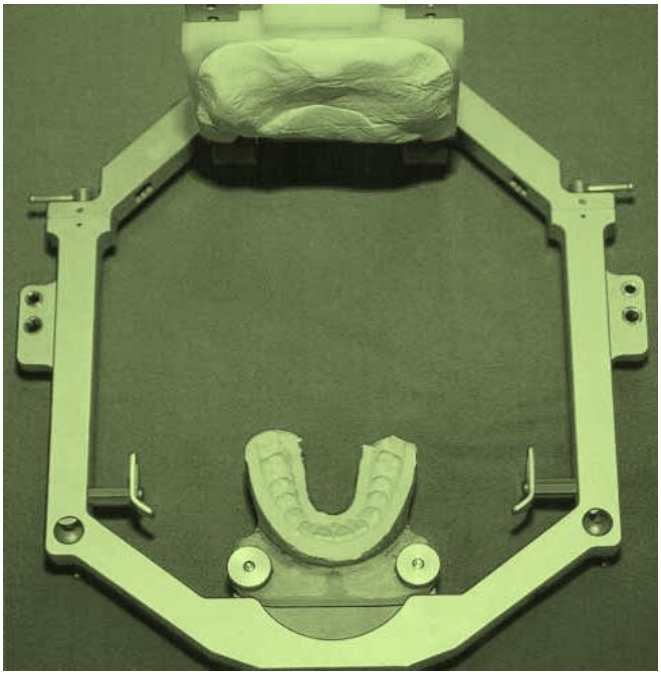


**Fig 2: GTC frame with dental impression and occipital pad**

**Fig 3: BRW localiser frame with nine rods**

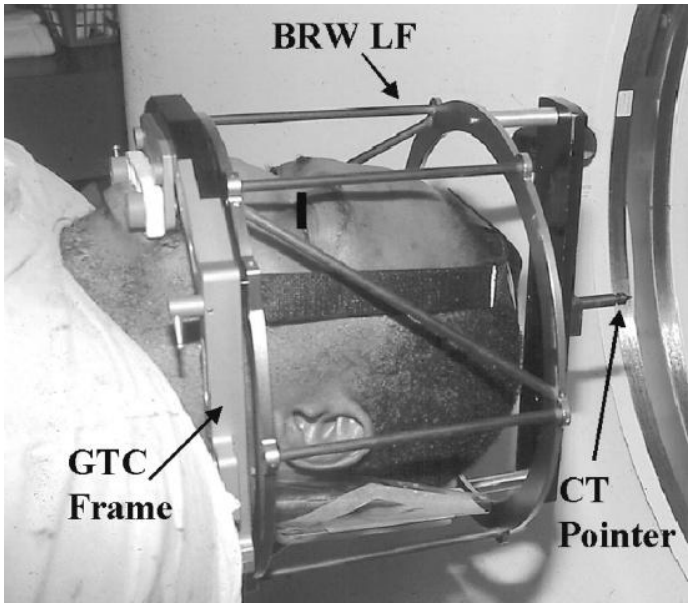



**Fig 4: Position of the patient during the planning CT scan using GTC frame and BRW localiser**

The same immobilisation is used during all the fractions of radiation. The GTC frame (Fig 5, 6) is fixed to the Linac Couch Mount Assembly (LCMA) during the treatment delivery. The Linac Target Locator Frame (LTLF) is attached to the GTC frame for patient positioning. The set-up lines on the LTLF should be aligned with the treatment room lasers

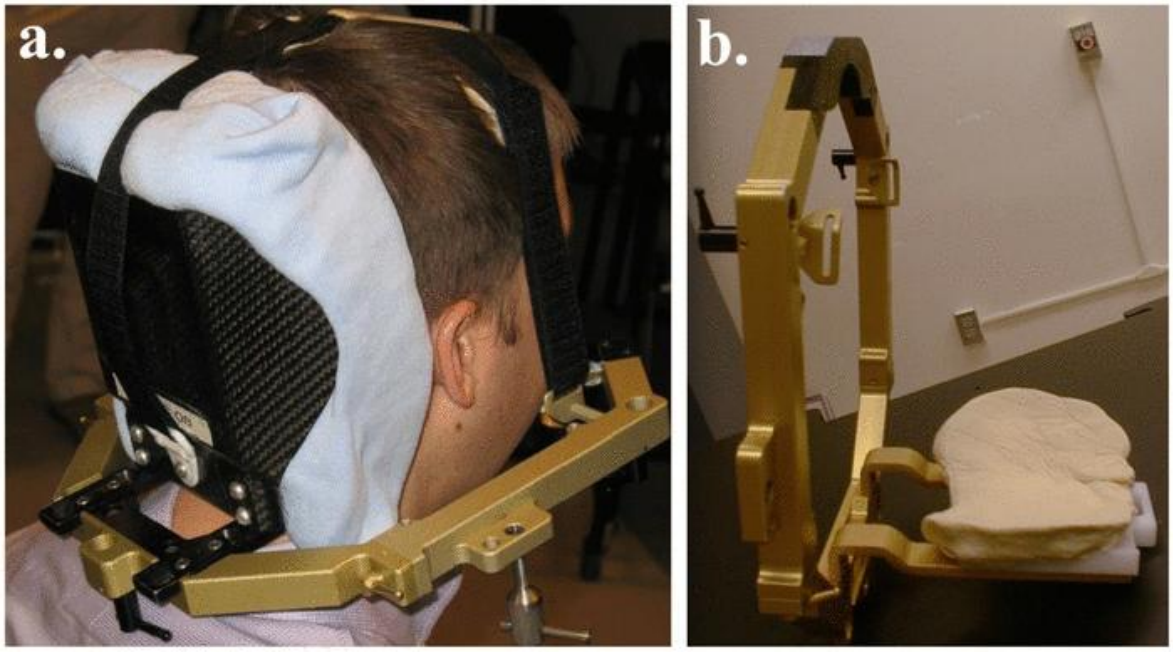



**Fig 5: Head frame fixed on the patient with head straps, which supports the weight**

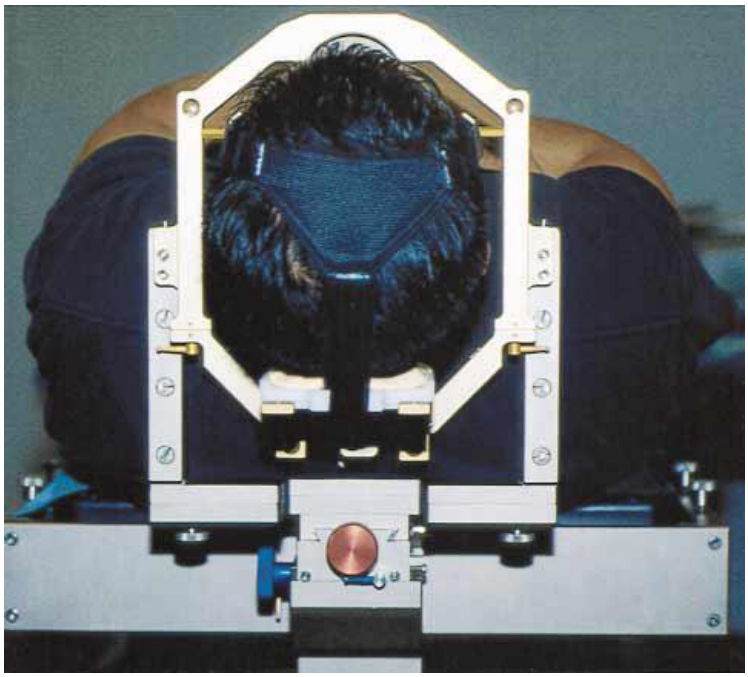


**Fig 6: Head frame attached to the treatment couch of the Linear Accelerator**

## 5.7 Different SRT techniques:

LINAC based SRT can be performed with different techniques, they are described here for the purpose of comparison of the three techniques. Initially LINAC based radiosurgery was started with "arc" based approach with circular collimator using a 4 MV linear accelerator at University of Southern California in 1986(5,44). Fixed circular collimators with projected size of the aperture ranging from 10-40 mm, typically using 4-8 arcs were used. Later multileaf collimators are used to shape the field depending on the target shape with advent of mMLC.

### 5.7.1 Static Conformal Field (SCF)

Selection of the static conformal fields depends on the consideration of both shape and location of the target as projected in the beam's eye view (BEV). Radiation fields can be designed using a single or multiple isocentres in coplanar or non-coplanar field arrangement. The aperture of each field is defined according to the shape of the target on to a plane perpendicular to the direction of the beam. Number of beams may vary depending upon the shape, location of the target with respect to surrounding normal structures and intended objective. Static conformal beams using of 5-9 numbers have been defined to achieve the target coverage. A margin of 2-3 mm is added during the planning to achieve the isodose coverage of the target(17).

## 5.8 Static Conformal Arc (SCA):

In this technique gantry moves around patient in a semi circular fashion resulting in a concentrated dose distribution in the target and minimal dose in the normal tissues.

The collimators are fixed in one of the beam's eye view of the target and the gantry is rotated around the patient. Number of arcs using three to six has been defined depending on the location, size, shape and intent of the therapy. Arcs may be used either in coplanar or in non-coplanar field arrangement (3).

### 5.8.1 Dynamic Conformal Arc (DCA):

The dynamic arc approach was initiated later after invention of the mMLCs. In this technique the gantry rotates around the target, during the dose delivery the shape of the miniature MLC is automatically adjusted to the projection of the target in beams eye view for every 10 degree increment from the gantry start angle(7). This additional option of shaping the mMLC while rotating gantry may result in high gradient conformal dose distribution (33,34).

## 5.9 Comparison of the various SRT techniques:

Many studies compare different techniques for linac based radiosurgical procedures. Bourland and McCollough *et al.*, found that conformal shaped fields using 7-11 beams resulted in the similar dose distribution as single isocentre circular arc technique(5). They also noted that, the adjacent normal structures can be easily shielded using conformal technique. However the peripheral dose distribution was higher for 7-11 field plans than for the circular fields. They further speculated that the dynamic MLC would make an advantage in reducing the peripheral dose.

Cardinale R et al. compared three stereotactic radiotherapy delivery techniques for the intracranial lesions using conventional linac system, non-coplanar shaped field and intensity modulated radiation fields(45). They suggested that arc technique is superior to the conformal shaped field technique in minimising the normal brain dose for the irregularly shaped target.

Solberg TD *et al.*,(46) made a comparison of the dynamic arc field shaping with static field conformal and non-coplanar circular arcs on simulated targets They have suggested that use of dynamic arc has an added advantage that they are simple to plan and fast to treat.

Evaluation of different radiosurgery techniques for pituitary adenomas was done by Grabenbauer GG *et al.*,(47) who compared the dynamic and conformal arcs, shaped beams and IMRT authors concluded that dynamic arc treatment with mMLC is considered safe and appropriate for treatment of pituitary adenomas.

Lee *et al.,* conducted a study to determine the effect of static and dynamic collimator optimization with use of microMLC in dynamic arc stereotactic radiotherapy on thirty patients with intracranial tumours(48) and concluded that dynamic collimator optimisation technique during the arc based therapy is an effective method in reducing the radiation dose to the peripheral normal brain. This method was also effective in improving the target conformity.

Hamilton *et a.,* evaluated the efficacy of static conformal fields with the use of multiple non-coplanar arcs for stereotactic radiosurgery or stereotactic radiotherapy in terms of dose delivery distribution and found that simple conformal therapy technique offers an advantage over multiple arc technique for SRS and SRT(49).

Sharma *et al,.* (50)compared the various conventional stereotactic (SRT) techniques with IM-SRT in brain tumours of varying shape, size, location and proximity to the organs at risk (OARs). They concluded that dynamic conformal arc (DCA) and static conformal field (SCF) are preferred SRT techniques in terms of target conformity and reduction of the dose to OARs.

### 5.10 Evaluation of the various SRT treatment techniques:

Every new technique of radiotherapy aims to widen the separation of the tumour control probability (TCP) and normal tissue complication probability (NTCP), along with uniform dose distribution throughout the target volume. The prescribed dose of radiation has to be distributed uniformly in the target volume.

The therapeutic advantage of high conformal radiotherapy depends on the conformity of the prescription dose to the planning target volume (PTV), dose homogeneity within the PTV, and less dose to the surrounding normal tissue and critical organs. The radiobiological effects and dose homogeneity are interrelated. The concept of equivalent uniform dose (EUD) developed by Niemierko *et al.,* (51)is one of the method helps in understanding relationship between the dose homogeneity and radiobiological effects. The equivalent uniform dose is defined as the biologically

equivalent dose that, if delivered uniformly, would lead to the same reduction in the tumour volume as the actual dose that has an inhomogeneous distribution.

The appropriate selection of the treatment plan depends on many factors, like dose distribution in the target, target coverage, presence of hot spots or cold spots and also the doses to the surrounding normal structures. Modern treatment planning systems generate enormous amount of data like maximum dose, mean dose, minimum dose and dose volume histograms. Radiation oncologist has to select the best plan based on information on clinical, radiologic, geometric, dosimetric, and radiobiologic parameters. Analysis with these tools may be more tedious and complex in deciding the optimal plan for patient. It is difficult to incorporate all the data in analysing these tools.

Different tools have been mentioned in the literature to analyse the radiotherapy treatment plan. The dose distribution in the plan can be visualized in the form of dose-volume histograms (DVHs), parameters like maximum dose ($d_{max}$), minimum dose ($d_{min}$), mean dose ($d_{mean}$) and modal dose delivered to each volume of interest. However these data may not clearly give idea in choosing the favourable plan all the time. RTOG guidelines used to analyse the treatment plan evaluation, by assessing the conformity index, homogeneity index and quality of the target coverage in addition to dose volume histogram.

### 5.10.1 Conformity index

The conformity index was developed to analyse the spatial dose distribution in each section of the target. It quantifies the degree of congruence between tumour contours and isodose lines by geometric intersection methods. This tool could facilitate the choice of a particular treatment and comparisons can also be made with different plans of the same patient for stereotactic radiotherapy. (52)

Conformity Index (RTOG) = $\frac{VRI}{TV}$

Where VRI reference isodose volume, and TV target volume.

The RTOG "conformity index" analyses the conformity based on the above mentioned formula. The RTOG conformity index 1 is an ideal form of conformation, where the reference isodose volume is exactly same as target volume. A conformity index greater than 1 indicates that the reference isodose volume is greater than the target volume; this represents irradiated volume is greater than the target volume and includes healthy tissues surrounding the target. If the conformity index is less than 1, the target volume is only partially covered by reference isodose or irradiated. It may be difficult to get conformity index of 1 in practical situations and rarely achieved, so RTOG guidelines, defined ranges of conformity index values to determine the quality of conformation.

If the conformity index is situated between 1 and 2, treatment is considered to comply with the treatment plan; an index between 2 and 2.5, or 0.9 and 1, is considered to be a

minor violation of the protocol, and an index less than 0.9 or more than 2.5 is considered to be a major violation of the protocol.

### 5.10.2 Homogeneity index

The concept of homogeneity index (HI) was developed to analyse the spatial dose distribution in each section of the treatment plan. HI was described as, (52)

$$HI_{RTOG} = \frac{Imax}{RI}$$

$I_{max}$ = maximum isodose in the target, and RI = reference isodose.

If the HI was ≤2, treatment was considered to comply with the protocol, if this index was between 2 to 2.5, it was considered as minor violation, but if the index exceeded 2.5, the violation of the protocol was considered to be major, but might nevertheless considered acceptable.

Reference isodose corresponds to either the minimum isodose volume containing the target volume or the 95% isodose volume according to ICRU 50 guidelines.

### 5.10.3 Quality of coverage

$$\text{Quality of coverage (RTOG)} = \frac{Imin}{RI} \text{ (52)}$$

Where I-min is minimum dose received by the target and RI is the reference isodose. As per the RTOG protocol, if the minimum dose received by the target is ≥90% of the

prescribed dose, the treatment is considered to be complying with protocol. If the minimum dose received by the target is 80-89% of the prescribed dose, the protocol is considered to be minor violation and if the minimum dose received by the target is <80% of the prescribed dose it is considered to be major protocol violation.

### 5.10.4 DVH Analysis

The large and more complex dosimetric data has to be analysed when a conformal plan is being evaluated and this prompted development of a tool which helps in understanding the frequency of dose distribution across the volume of the interest, known as dose volume histogram (53). Two types of DVH have been defined; the differential DVH (dDVH) and the integral DVH (iDVH). They both are useful for assessing tumor volume coverage and the dose distribution either to healthy tissue surrounding the target or to specific structures in the vicinity of the target.

The DVH is thus a powerful tool used for conformal plan evaluation. The plan can be analysed in terms of DVHs for PTV or PRVs and OARs. Several plans of a same patient can be compared and analysed using DVH analysis. However DVH does not give information on the spatial dose distribution, but provides volume based information for summarizing and quantifying complex dose distributions. It also provides an accurate assessment of homogeneity in the PTV.

## 5.11 Normal tissue tolerances

The following are the normal tissue tolerances, as defined in the Quantitative Analyses of Normal Tissue Effects in the Clinic (QUANTEC) (54,55). These guidelines are considered here for the treatment of the tumours with conventional fractionation schedules with respect to volume and dose to a particular organ and their expected toxicity (Table 5-1).

**Table 5-1 Normal tissue toxicity profile of as per QUANTEC guidelines**

| Normal tissue toxicity profile of as per QUANTEC guidelines | | | | | |
|---|---|---|---|---|---|
| Critical Structure | Volume | Dose/Volume | Max Dose | Toxicity Rate | Toxicity Endpoint |
| Brain stem | The entire brain stem can be treated upto 54Gy | | <54 Gy | <5% | Neuropathy or necrosis |
| Brain stem | D1-10 cc | ≤59 Gy | | <5% | Neuropathy or necrosis |
| Brain stem | | Maximum point dose | <64 Gy | <5% | Neuropathy or necrosis |
| Optic nerve/chiasm | | Maximum point dose | <55 Gy | <3% | Optic neuropathy |
| Optic nerve/chiasm | | Maximum point dose | 55-60 Gy | 3-7% | Optic neuropathy |
| Optic nerve/chiasm | | Maximum point dose | >60 Gy | >7-20% | Optic neuropathy |
| Brain | To partial brain | | <60 Gy | <3% | Symptomatic necrosis |
| Brain | To partial brain | | 72 Gy | 5% | Symptomatic necrosis |
| Brain | To partial brain | | 90 Gy | 10% | Symptomatic necrosis |

## 5.12 Pituitary adenoma

Pituitary adenomas are tumours that occur in the pituitary gland. Based on pathology, pituitary adenomas are divided into three categories, benign adenoma, atypical adenoma (invasive adenoma) and carcinomas. Pituitary carcinomas accounts for 0.1% to 0.2%, whereas invasive adenomas accounts for approximately 35% remaining being benign adenomas (56).

### 5.12.1 Epidemiology

Tumors of the pituitary gland and sellar region represent approximately 10-15% of all brain tumors, of which the great majority in this region are pituitary adenomas (11). Majority of the pituitary tumours are undiagnosed and are often found at autopsy.

The incidence of macroadenomas is similar in males and females. Symptomatic prolactinomas and Cushing disease are found more frequently in women. Most pituitary tumors seen in young adults, but they may be seen in adolescents and elderly persons. Acromegaly usually is seen in the fourth and fifth decades of life.

In a population based study in England of a single community the prevalence of the pituitary adenomas per 100,000 was as follows (11).

| | |
|---|---|
| All adenomas | 77.6 |
| Lactotroph adenomas | 44.4 |
| Non-functioning adenomas | 22.2 |

| | |
|---|---|
| Somatotroph adenomas | 8.6 |
| Corticotroph adenomas | 1.2 |

### 5.12.2 Anatomy

Pituitary gland (Fig 7,8) is a midline structure, measures about 15mm in antero-posterior and 12mm in craniocaudal axis. Pituitary gland is located in the sella turcica (hypophysial fossa) which is a part of the sphenoid bone. Pituitary gland is related superiorly to optic chiasm; inferiorly to inter cavernous venous sinus & sphenoid air sinus. Transsphenoidal approach through nose is a surgical technique performed to resect the tumour through sphenoid air cells.

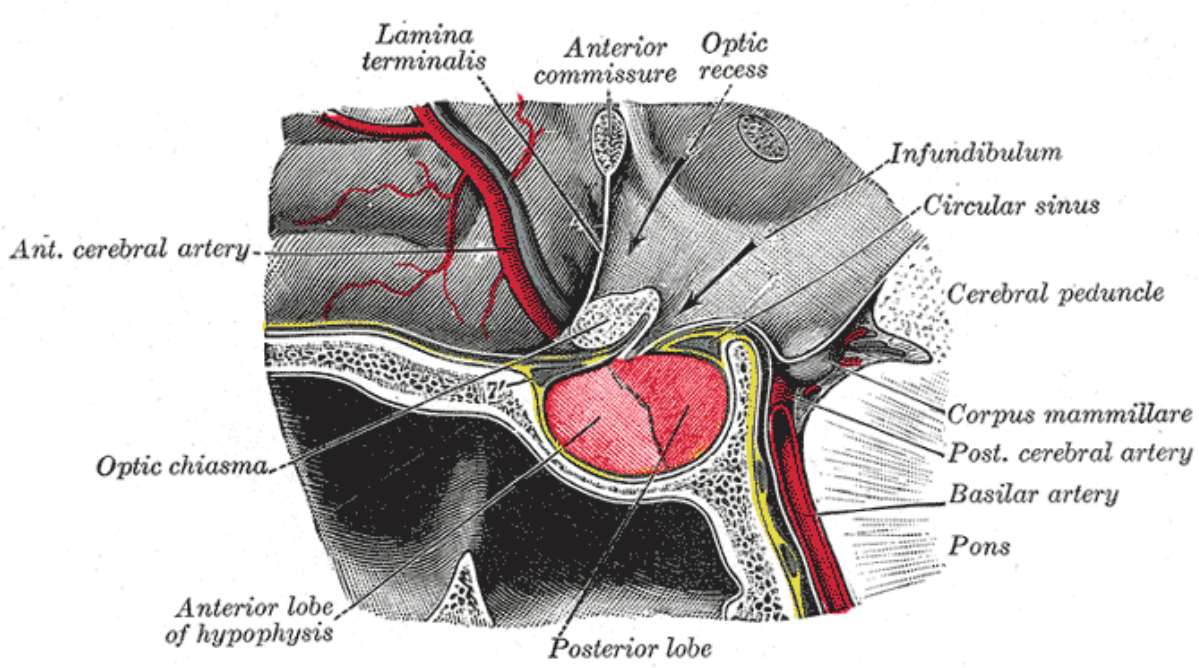



**Fig 1: Anatomy of the pituitary gland**

### 5.12.3 Clinical presentation

Pituitary adenomas can present with symptoms of hormonal abnormalities or of local tumour growth leading to pressure effects. A pituitary adenoma may also present with non-specific headache, visual field defects, because of the pressure effects of the tumour. The most common field defects are classically bitemporal hemianopia and superior temporal quadrantanopia (57).

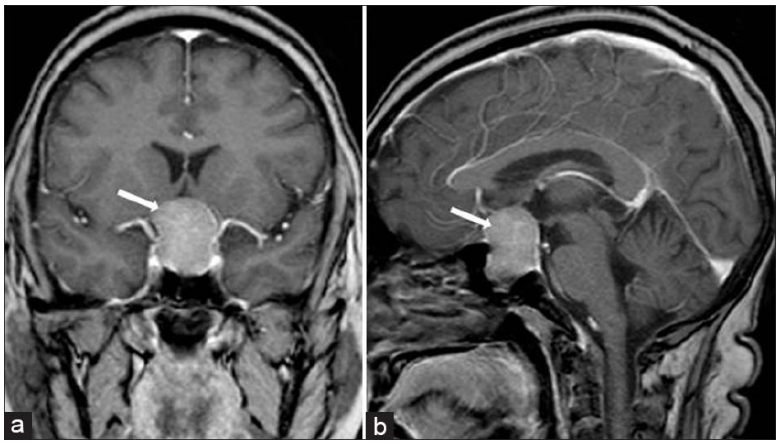



**Fig 2; MRI image showing Pituitary adenomas, a. Coronal view, b. Sagittal view**

### 5.12.4 Management

#### *5.12.4.1 Overview:*

Pituitary adenoma should be managed with multidisciplinary team including disciplines of neuroradiology, endocrinology, neurosurgery, radiation oncology and pathology. The goal of the treatment of Pituitary adenomas includes the assessment of accurate tumour extent, correction of the hormonal abnormalities; relieve pressure effects while minimising the injury to the surrounding normal structures (58).

Observation is an option for non-secreting microadenomas and small asymptomatic prolactinomas. If asymptomatic microadenomas are not treated, these patients can be observed with annual imaging studies.

#### *5.12.4.2 Medical management*

Medical management is mainstay of treatment in Prolactinomas and its role has been established in controlling the hormonal hypersecretion even in other secreting adenomas. Initially most Prolactinomas are managed with Dopamine agonists such as Bromocriptine, Pergolide or Lysuride. Medical intervention may reduce the size of the tumour and decrease the function. (58)A Somatostatin analogue, Octreotide is used as adjunctive therapy for medical management of pituitary growth hormone secreting adenomas(59). Growth hormone receptor antagonist Bromocriptine has also been widely used in treating Acromegaly(60). Newer growth hormone receptor antagonist Pegvisomant is also used for long term hormonal control (61).

#### *5.12.4.3 Surgical management*

The standard surgical approach for most of the pituitary adenomas is transsphenoidal microsurgery(62), which accounts for more than 95% of the procedures and rarely craniotomy is performed. This approach is safe and normalises the hormonal levels and relieves the pressure symptoms.

#### *5.12.4.4 Radiation therapy*

Radiation therapy of pituitary adenoma is highly effective. It is recommended after subtotal resection of primary tumors such as macroadenomas, after gross total resection of endocrine active adenomas with postsurgical hormone secretion and for recurrent tumors. Radiation therapy is also choice of treatment in patients who cannot undergo surgery due to co morbidities (63).

Radiation is delivered using a total dose of around 45Gy or 5040cGy in 1.8Gy daily dose fractionation(15). Normalisation of the hormonal levels can take months to years after radiation therapy(16). Radiation therapy is effective in controlling the tumour growth in as high as 90-100% in many series regardless of the type of adenoma and technique of radiation used. The toxicities related to the radiation are generally low (15).

#### *5.12.4.5 The choice of radiation therapy*

The choice of radiation therapy to pituitary adenomas depends on the availability of the particular technique of radiation, physician preferences and perceived differences associated with each technique rather than the differences in clinical outcomes. The various modalities of delivering radiation include two dimensional external beam radiation therapy, conformal radiation therapy (3DCRT), fractionated stereotactic radiotherapy and proton beam radiation therapy.

#### *5.12.4.6 Stereotactic radiotherapy*

In the past, Pituitary adenoma was treated with conventional radiotherapy(64). Because of the proximity of the organs at risk like, optic nerves, chiasm and brain stem, SRT is the preferred radiotherapy technique. Though impressive outcomes with stereotactic radiosurgery(SRS) using Gamma Knife have been reported by many(64) it may not be suitable to deliver high single fraction radiation for tumours that are large and tumours that are very close(<3-5mm) to optic pathways as dose limitation to optic apparatus is 8-10Gy in single fraction(50,51,65) Whereas stereotactic radiation with multiple fractions of standard dose per fraction allows sensitive surrounding normal structures to repair and regenerate during the course of radiation. This has benefit of a radiobiologial advantage over the radiosurgery, especially for the structures like optic apparatus, which has a low $\alpha/\beta$ ratio ($\leq$3 Gy) (21). More recently many reports indicated promising outcomes with SRT(16).

## 5.13 Craniopharyngioma

The incidence of newly diagnosed craniopharyngiomas ranges from 0.13 to 2 per 100,000 population per year (66). Presentation is equal in both sexes with bimodal age distribution. In children the peak incidence is around of 5-14 years where as in adults' common age at presentation is in the age range of 65-74 years. Craniopharyngiomas accounts for 5% of all tumours in children and 50% of all sellar/para sellar tumours (66).

Craniopharyngioma is located in the suprasellar region and anatomically these tumours are in close proximity with the optic apparatus and brain stem. Craniopharyngiomas are histologically benign tumours. Craniopharyngioma arises from epithelial remnants of the Rathke pouch in the suprasellar region(67).

Craniopharyngioma is diagnosed mainly by clinical (neurological and endocrine symptoms) and radiological (Fig 9) (a calcified solid/cystic mass) findings. The diagnosis is confirmed by characteristic histological findings, of numerous microcysts. Tumour may also be associated with hyalinised calcified structures, foreign body giant cells and occasionally clefts having cholesterol granules. Craniopharyngioma may present with hormonal abnormalities due to compression of the pituitary or hypothalamus. Lesion in the pre chiasmal area may compress the optic pathway, leading to visual field defects or decreased visual acuity, whereas retro chiasmal lesions may grow in to the third ventricle causing hydrocephalus or compression of the optic tracts.

**Fig 3: MRI imaging of a patient diagnosed with Craniopharyngioma, from clockwise, T1W Post gado coronal, T1W sagittal and T2W transverse images on the lower side**

Management options of Cranipharyngioma include complete resection or subtotal resection followed by observation. External beam radiation therapy is indicated for recurrent disease or subtotal resection of the tumour

Stereotactic radiotherapy (SRT) is considered as the technique of choice for radiation in these patients because it allows the precise delivery of high-dose radiation to the tumour, while minimizing irradiation of surrounding critical structures (68). Daniela and Ertner *et al.,* in a retrospective series have reported that, SRT using a Linear accelerator in Craniopharyngioma is safe and toxicity is extremely low. Visual acuity was improved in 5/12 patients and there was no new visual impairment during the follow up post SRT. After SRT only one out of 12 patients developed panhypopituitarism while 6/12 developed partial hypopituitarism (68).

Stephanie E. Combs, *et al*., reported excellent long-term outcome for Craniopharyngiomas with regard to local control as well as treatment-related side effects using linear accelerator based SRT (69).

### 5.14 Radiation induced Second cancer and Cognitive functions

Risk of secondary cancer information comes from general population comes from Atomic bomb survivors and patients who are treated with radiotherapy. Studies on survivors of atomic bomb have shown that the risk increases linearly up to 2Sv. Risk of radiation induced cancers for several organs increases substantially at doses far above 2Gy(70). Though the incidence of cancer risk may be low but its a very serious and potentially fatal late complication of radiation. In a retrospective study by Nishio *et al.*, (71) 11 patients who received therapeutic cranial irradiation with dose range of 24-110Gy (is this dose range correct) (median of 54 Gy) to their primary disease developed secondary tumours within the span of 13 years. All the tumours were in the

field of previous radiation and satisfied with definitions of Radiation induced neoplasms. Patients tend to be young (1.3-42 years; median age of 22 years) and the median latency period was 14.5 years.

Erridge *et al.,* (13) in an audit on patients with pituitary adenoma treated with radiotherapy reported a good long term control of tumour with increased risk for intra-cranial tumours with radiation. The 20-year actuarial risk 1.9% (CI 0–2.6%), and a relative risk of 5.65 (0.53–20.77, $p = 0.10$) of men and 9.94 (0.94–36.56, $p = 0.04$) women observed. Risk of secondary brain tumour risk was 1.9% at 20 years in a study by Michel Brada on pituitary tumours (72).

Neglia *et al.,* (73) et al have studied incidence of occurrence of subsequent primary central nervous system (CNS) tumours as a late event in children treated for leukemia or brain tumours on 14361 patients. Subsequent CNS primary neoplasms were diagnosed in 116 individuals. Gliomas (n=40) occurred after a median of 9 years and meningiomas (n=66), after a median of 17 years. The dose response for the excess relative risk was linear for both meningiomas and gliomas. Highest risk was found in children exposed less than 5 years of age. Radiation dose response relationship was highly statistically significant ($P<0.001$) for all CNS tumors. Odds ratios for glioma rose sharply across the radiation categories and it was highest (21-fold) for doses of 30-44.9Gy. Highest risk of radiation induced secondary cancers was found in patients who received more doses, who survived longer and at young age.

Reimers *et al.*, (74) described association between cognitive outcomes in survivors of the 133 childhood CNS tumours. The mean intelligence (IQ) scores were substantially lower than the expected means of the general population, the patients treated with RT found to be significantly affected. Radiation therapy was found to be most important risk factor for the impaired cognitive functions. The mean observed full scale IQ was 97.1 (SD = 14.3) for the non-irradiated patients and 78.8 (SD = 14.3) for the irradiated patients ($P < 0.001$).

In a study by Guinan *et al.*, (75) on cognitive effect of the pituitary tumours and their treatment on cognitive effects, have shown memory was more severely affected in patients who had received adjuvant radiation.

# METHODOLOGY

# 6 METHODOLGY

## 6.1 Setting

The planning CT image sets of patients who had undergone stereotactic radiotherapy (SRT) for pituitary adenoma or craniopharyngiomas were used in this study. Twenty such patient data sets were available in the iPlan brain lab data system from April 2014 to August 2015. These data sets were included in our study. CT image sets were used to generate three separate plans with three separate techniques (SCF, SCA and DCA respectively) and these plans were compared across for various parameters as mentioned below.

## 6.2 Participants

The study was carried out on image sets acquired on patients with Craniopharyngioma and Pituitary adenoma and who had received SRT. The SCF plans were already generated for treatment using Brain LAB, iPlan RT V.4.5.3 Germany, Treatment Planning System (TPS) software and treated with Clinac-DMX 2100-CD linear accelerator Varian, Palo Alto, CA.

## 6.3 Inclusion criteria

The patients with biopsy proven diagnosis of either Craniopharyngioma or Pituitary adenoma who have been treated with SRT in department of radiotherapy unit 1 from April 2014 to August 2015 were selected for the study. Fractionated SRT was performed using a Clinac-DMX 2100-CD linear accelerator Varian, Palo Alto, CA.

The plans were initially generated under Brain LAB, iPlan RT V.4.5.3 Germany; Treatment Planning System (TPS) were selected.

### 6.4 Exclusion criteria:

Image sets of the patients with other histologies.

### 6.5 Sample size:

Since the study being pilot study, the sample size was chosen to be 20.

### 6.6 Source:

Department register having the details of the patients who were treated with SRT were searched from April 2014 to August 2015. Image sets of patients with Pituitary adenoma and Craniopharyngiomas treated with linear accelerator based SRT techniques were selected. The image sets were available in Brain LAB, iPlan RT V.4.5.3 Germany, Treatment Planning System (TPS).

### 6.7 Selection Method:

The images sets of 20 consecutive patients treated for Pituitary adenoma or Craniopharyngioma were taken for the study retrospectively and prospectively. The patient selection involves the search of the patients who have been treated in the during the period April 2014 to August 2015 who were treated under Unit I of radiotherapy department, Christian medical college, Vellore, Tamil Nadu, India. All the patients underwent the process of planning CT using GTC frame and a BRW

localiser system. All the patients in the eligible population source were selected and assigned a unique identification number.

## 6.8 Consent

This study is a type of observational study performed on the image sets of patients diagnosed to have Pituitary adenoma and Craniopharyngioma. This data containing CT image was available in the Brain LAB, iPlan RT V.4.5.3 Germany, Treatment Planning System (TPS) archives and conformed to the patient confidentiality and norms for the electronic data. So the consent waiver was applied for and this was accepted by our Institutional Review Board scientific and ethics committee.

## 6.9 List of materials used for this study:

The following were used to perform this study, Treatment planning system:

- Treatment planning system
- Patient's image data sets
- Linear accelerator
- Phantom

#### *6.9.1.1 Treatment planning system*

In our department we have VARIAN MEDICAL SYSTEMS, Inc, CLINAC (Linear accelerator) and Brain LAB, iPlan RT V.4.5.3 Germany, Treatment Planning System (TPS) which is regularly used for the treatment of the patients for stereotactic

radiotherapy. The same software was used for the image registration, localisation, delineation of the tumours and organs at risk. The beam placement, plan generation, calculation of the dose, generation of the dose volume histograms were done after the delineation of the structures. CLINAC the Linear Accelerator, used regularly for the treatment of these patients, was used to analyse the efficacy of the plans on a phantom.

The study utilised the Brain LAB, iPlan RT V.4.5.3 Germany, Treatment Planning System (TPS) configured with dose calculation and treatment delivery algorithms of Varian CLINAC(TM) 6 MV (Megavoltage) photon beam, the Radionics Brown Robert Wells stereotactic frame and Brain lab m3 micro multileaf collimator.

#### *6.9.1.2 Patient's data image data sets*

The image sets are the planning CT scan images of the patients performed during the time of SRT treatment. These data sets were available in the TPS and same image sets are used for the delineation of GTV and normal organs and planning purposes.

#### *6.9.1.3 Linear Accelerator*

Linear accelerator is megavoltage x-ray generator by accelerating the charged particles. Clinac-DMX 2100-CD linear accelerator Varian, Palo Alto, CA is available in our department for the purpose of treatment of the patients. Same machine is used here to assess the plans.

#### *6.9.1.4 Phantom*

Phantom is a models of human body used in dosimetric studies of the ionising radiation. We use water phantom in this study to measure the time required to deliver the prescribed radiation for one patients plan.

## 6.10 Contouring

Patient's planning computed tomography datasets, with 3-mm-slice thickness from vertex to lower border of second cervical vertebra was retrieved from the Brain LAB, iPlan RT V.4.5.3 Germany, Treatment Planning System (TPS) for computation of treatment plans. The image data sets of patients with pituitary adenoma and craniopharyngioma who underwent planning CT simulation with Gill Thomas Cosman stereotactic localizing frame along with BRW localiser system form April 2014 to August 2015 were selected for contouring. The same image data sets were used for all the three treatment techniques.

The gross tumour volume (GTV) was contoured by the Neurosurgeon for all these patients at the time of initial planning for SRT. The GTV was outlined on axial CT fused with axial T1 Gadolinium magnetic resonance images. The planning target volume was given by a radiation oncologist by expanding the GTV by 3 mm in all directions. The Organs at risk (OAR) were contoured by the radiation oncologist or Neurosurgeon.

## 6.11 Method of generating the SRT plans.

Each patient will have three plans using the same PTV and OARs; SCF, SCA and DCA. For ease of dosimetric analysis, we prescribed a uniform dose (54Gy in 30 fractions) to all planning target volumes (PTV) irrespective of the diagnosis. Treatment planning system (TPS) Brain LAB, iPlan RT version 4.5.3 uses the pencil beam algorithm with tissue inhomogeneity correction to calculate the dose distribution. The grid size for calculation was 2-mm pixel. The same dose requirements for PTV (minimum of 95%) coverage and OAR sparing were set for all the three techniques. All the treatment planning was done by one physicist with a supervision of the senior physicist to minimize interoperator variations. Moreover, all plans were verified by radiation oncologist to ensure that the quality of each plan met the required standard.

The treatment plan was performed by the medical physicist using the same PTV for all the plans. All the plans were performed under Brain LAB, iPlan RT V.4.5.3 Germany, Treatment Planning System (TPS) software.

For SCF plan single isocenter with 3 to 7 noncoplanar beams were used. Beam shaping was tailored by the brainlab 3mm micro MLCs. The static conformal beam technique uses non-coplanar uniform static fields, defined by the beam's eye view projections of the target volume, and directed to a single isocenter. To produce these plans, the treatment isocenter was first placed at the geometric centre of the target. Then, the beams were entered in various directions so as to minimize the overlap

between the entrance and exit beam paths. A margin of around 3mm was added to each beam in order to have approximately the 95% (of the maximum dose) isodose surface completely encompassing the target volume. The collimator angle was always optimized in order to irradiate the smallest possible area for each beam.

Static conformal arc was planned with 3-6 arcs in a non coplanar fashion with single isocentre. The dynamic conformal arc was planned similarly as in the static arc technique, but in the case dynamic arc technique mMLCs fit to the shape of the beam's eye view every 10 degree gantry movement from the starting angle till the end.

## 6.12 Dosimetric Comparison of the three plans

Dosimetric analysis was performed using DVHs and 2D dose displays, RTOG quality assurance guidelines of SRT like conformity index(CI), homogeneity index(HI) and quality of target coverage. Analysis of plans was also performed using parameters like maximum dose, minimum dose and mean dose to the target, dose received by OARs and the volume of brain receiving 5Gy, 6Gy, 10Gy, 20Gy and 40Gy.

### 6.12.1 Conformity index:

The RTOG "Conformity index" analyses the conformity based on the formula,

Conformity Index (RTOG) = $\frac{VRI}{TV}$

Where VRI reference isodose volume and TV is target volume.

The RTOG conformity index 1 is an ideal form of conformation, where the reference isodose volume is exactly same as target volume. A conformity index greater than 1 indicates that the reference isodose volume is greater than the target volume; this represents irradiated volume is greater than the target volume and includes healthy tissues surrounding the target. If the conformity index is less than 1, the target volume is only partially covered by reference isodose or irradiated. It may be difficult to get conformity index of 1 in practical situations and rarely achieved, so RTOG guidelines, defined ranges of conformity index values to determine the quality of conformation. If the conformity index is between 1 and 2, treatment is considered to comply with the treatment plan; an index between 2 and 2.5, or 0.9 and 1, is considered to be a minor violation of the protocol, and an index less than 0.9 or more than 2.5 is considered to be a major violation of the protocol.

**6.12.2 Homogeneity index:**

The concept of homogeneity index (HI) was developed to analyse the spatial dose distribution in each section of the treatment plan. HI was described as per the RTOG,

$HI_{RTOG} = \frac{Imax}{RI}$, where,

$I_{max}$ = maximum dose received by the target, and RI = reference isodose (95% isodose). If the HI was ≤2, treatment was considered to comply with the protocol, if this index was between 2 to 2.5, it was considered as minor violation, but if the index

exceeded 2.5, the violation of the protocol was considered to be major, but might nevertheless considered acceptable(90).

### 6.12.3 Quality of coverage

Quality of coverage was calculated using formula as described in the RTOG,

Quality of coverage (RTOG) = I min/RI

Where I-min is minimum dose received by the PTV and RI is the reference isodose (reference isodose was taken as 95% of the prescribed dose).

For the quality coverage as in formula 1, if the minimum dose received by the PTV is 90 % of the prescribed dose, the treatment plan is considered to be complying with protocol. If the minimum dose received by the target is between 80 to 89% of the prescribed dose, the protocol is considered to be minor violation. If the minimum dose received by the target is less than 80 % of the prescribed dose, it is considered to be major protocol violation.

### 6.12.4 Organs at risk

For the OARs, maximum dose was compared across three plans.

The volume of brain receiving 5Gy, 6Gy, 10Gy, 20Gy and 40Gy was compared across three plans for all the patient data sets. This helped us in selection of a better SRT technique with regard to spillage of lower dose.

### 6.12.5 Treatment Time

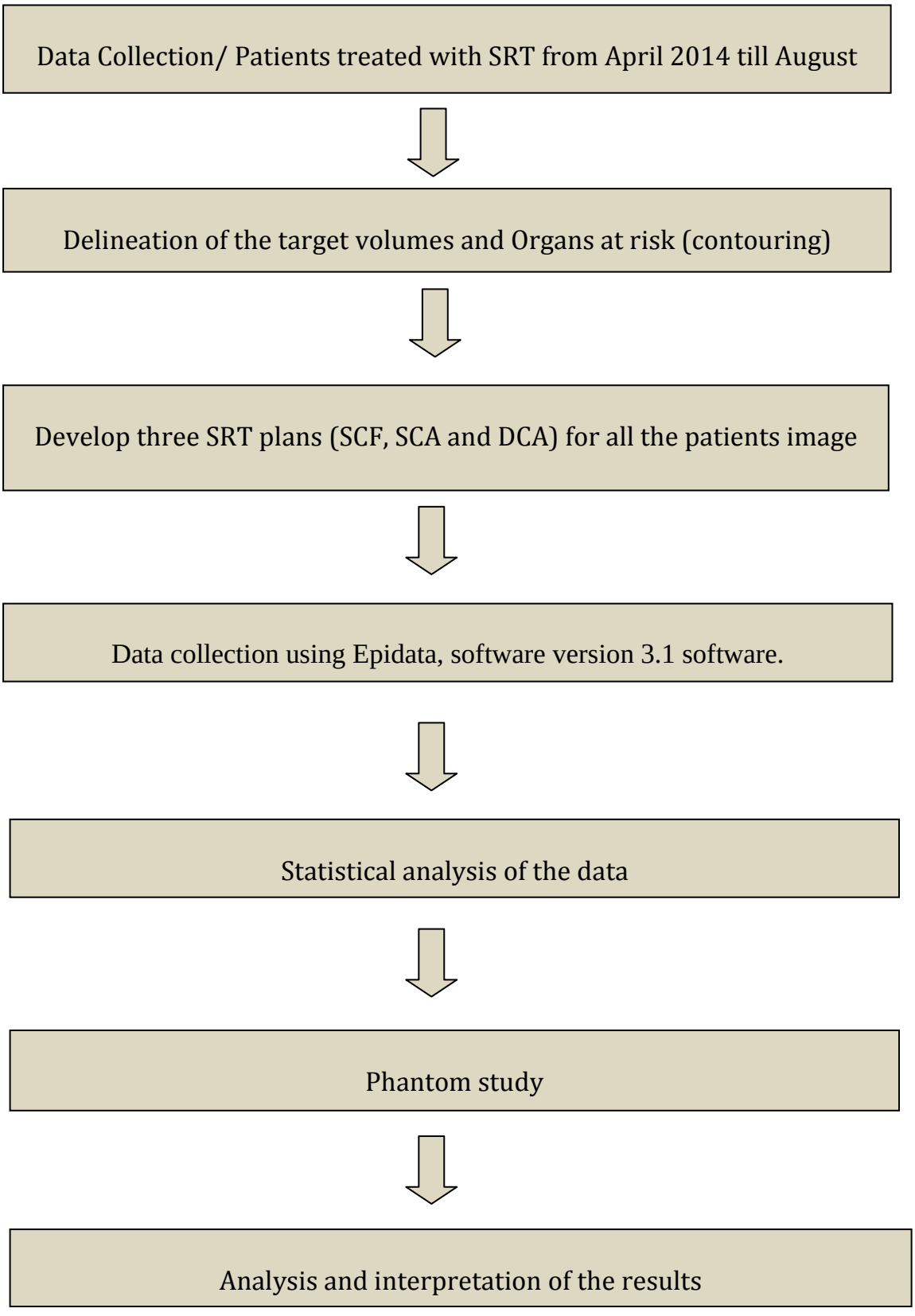
We estimated the time taken for to deliver the intended radiation dose for all the three plans for 2 patient data sets. The time taken for positioning of the patient for the treatment, frame fitting and adjustment were considered to be constant for all the three plans. However the time taken to deliver radiation, isocentre matching with room lasers, number of monitor units may differ. So treatment plans are analysed in terms of time taken to deliver each fraction of RT and initial time taken for verification purpose.

## 6.13 Statistical analysis:

Data entry was done in Epidata version 3.1 and was analysed using SPSS 17.0 (Statistical Package for social sciences). For continuous data, the descriptive statistics such as n, mean, standard deviation, median, minimum and maximum was represented. For categorical data, the number of patient data sets and percentage was presented.

Based on the normality of the data the parametric ANOVA test or non parametric Kruskal Wallis test was used to compare the three stereotactic radiotherapy treatment techniques.

## 6.14 Detailed diagrammatic Algorithm of the study



# RESULTS

# 7 RESULTS

## 7.1 Patient Characteristics

Patients' age ranged from 6 to 77 years with the median age of 33 years. Twelve patients were diagnosed to have Pituitary adenoma and 8 with Craniopharyngioma. For dosimetry purposes the dose prescribed was 5400cGy in 30 fractions in all the plans for all data sets. The characteristics of the patients are listed in the Table 7.1

**Table-7-1Patient Characteristics**

| Serial No | Age in years | Gender | Diagnosis | PTV Vol. in cc |
|---|---|---|---|---|
| 1 | 33 | Female | Pituitary adenoma | 11.24 |
| 2 | 55 | Male | Pituitary adenoma | 12.91 |
| 3 | 16 | Female | Craniopharyngioma | 06.47 |
| 4 | 11 | Female | Craniopharyngioma | 12.66 |
| 5 | 36 | Male | Pituitary adenoma | 07.62 |
| 6 | 13 | Male | Pituitary adenoma | 14.45 |
| 7 | 48 | Female | Craniopharyngioma | 13.67 |
| 8 | 13 | Female | Craniopharyngioma | 15.13 |
| 9 | 38 | Male | Pituitary adenoma | 14.38 |
| 10 | 75 | Female | Pituitary adenoma | 25.06 |
| 11 | 33 | Female | Pituitary adenoma | 16.32 |
| 12 | 77 | Male | Pituitary adenoma | 11.45 |
| 13 | 47 | Male | Pituitary adenoma | 41.61 |
| 14 | 6 | Male | Craniopharyngioma | 23.94 |
| 15 | 28 | Female | Pituitary adenoma | 22.02 |
| 16 | 7 | Female | Craniopharyngioma | 49.15 |
| 17 | 39 | Female | Pituitary adenoma | 14.51 |
| 18 | 67 | Male | Pituitary adenoma | 11.79 |
| 19 | 32 | Female | Craniopharyngioma | 23.49 |
| 20 | 6 | Male | Craniopharyngioma | 34.28 |

## 7.2 Planning Target Volume

The planning target volume ranged from 6.47cc to 49.15cc, with a median PTV of 14.48cc. Fig. 10 represents the volume of PTV in all the patients. Thirteen patients had PTV <20cc and 7 had >20cc volume.

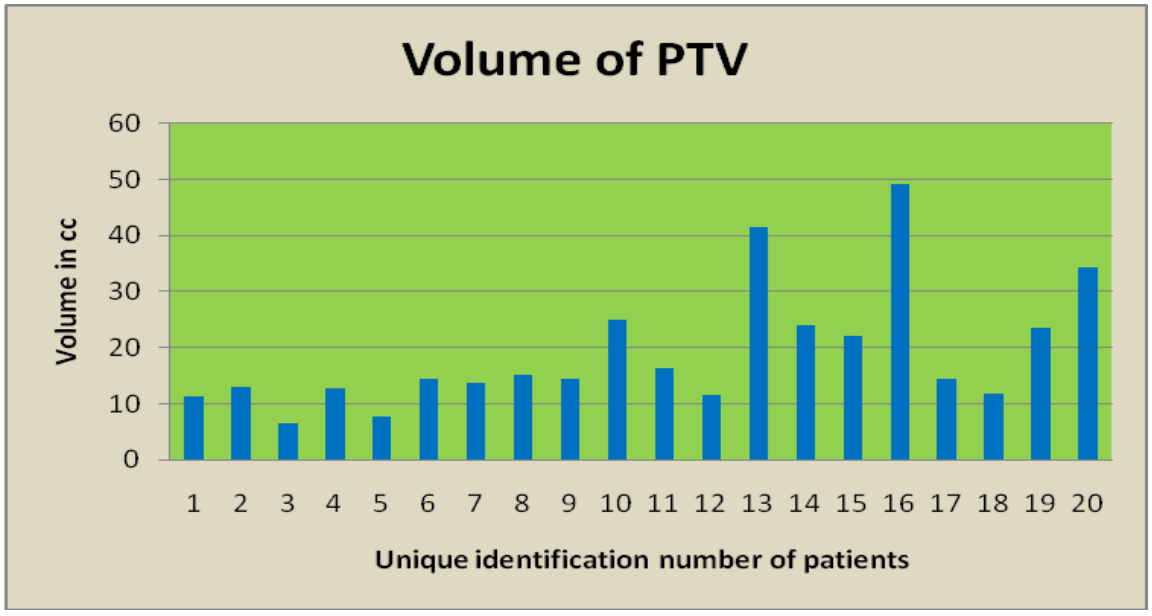



**Fig 4: PTV volumes for 20 patient data sets**

## 7.3 Reference Isodose Volume

Reference isodose volume was taken as the volume covered by 95% isodose line. The volume of the 95% isodose was generated and volume was measured in cc.

**Table 7-2 Planning Target Volume and corresponding Reference Isodose Volumes of three SRT techniques**

| Reference Isodose Volume | | | | |
|---|---|---|---|---|
| S no | Volume of PTV | SCF | SCA | DCA |
| 1 | 11.24 | 17.06 | 14.52 | 16.69 |
| 2 | 12.91 | 15.35 | 16.39 | 17.86 |
| 3 | 6.47 | 9.43 | 9.21 | 8.93 |
| 4 | 12.66 | 20.65 | 18.78 | 21.67 |
| 5 | 7.62 | 10.76 | 10.38 | 10.52 |
| 6 | 14.45 | 19.02 | 19.75 | 20.59 |
| 7 | 13.67 | 20.16 | 16.18 | 17.16 |
| 8 | 15.13 | 16.54 | 22.01 | 21.96 |
| 9 | 14.38 | 17.06 | 17.56 | 17.19 |
| 10 | 25.06 | 29.40 | 34.63 | 32.23 |
| 11 | 16.32 | 20.63 | 20.99 | 20.84 |
| 12 | 11.45 | 13.78 | 15.61 | 13.36 |
| 13 | 41.61 | 66.65 | 57.30 | 50.72 |
| 14 | 23.94 | 26.68 | 30.12 | 28.70 |
| 15 | 22.02 | 34.43 | 32.62 | 27.20 |
| 16 | 49.15 | 60.59 | 68.62 | 63.84 |
| 17 | 14.51 | 19.18 | 19.43 | 17.83 |
| 18 | 11.79 | 20.72 | 20.65 | 20.60 |
| 19 | 23.49 | 26.96 | 27.96 | 29.36 |
| 20 | 34.28 | 42.23 | 39.9 | 42.86 |
| Mean + SD | 19.11 ± 11.21 | 25.36 ± 15.25 | 25.63 ± 15.14 | 25.01 ± 13.67 |
| p Value | 0.062 | | | |

*SCF=Static Conformal Field, SCA=Static Conformal Arc and DCA=Dynamic Conformal Arc*

Average volume of the reference isodose was around 25cc in all the three plans however there was a minimal reduction in this volume in the DCA compared to SCF and SCA plans. The values are presented in Table 7.2 and Fig 11.

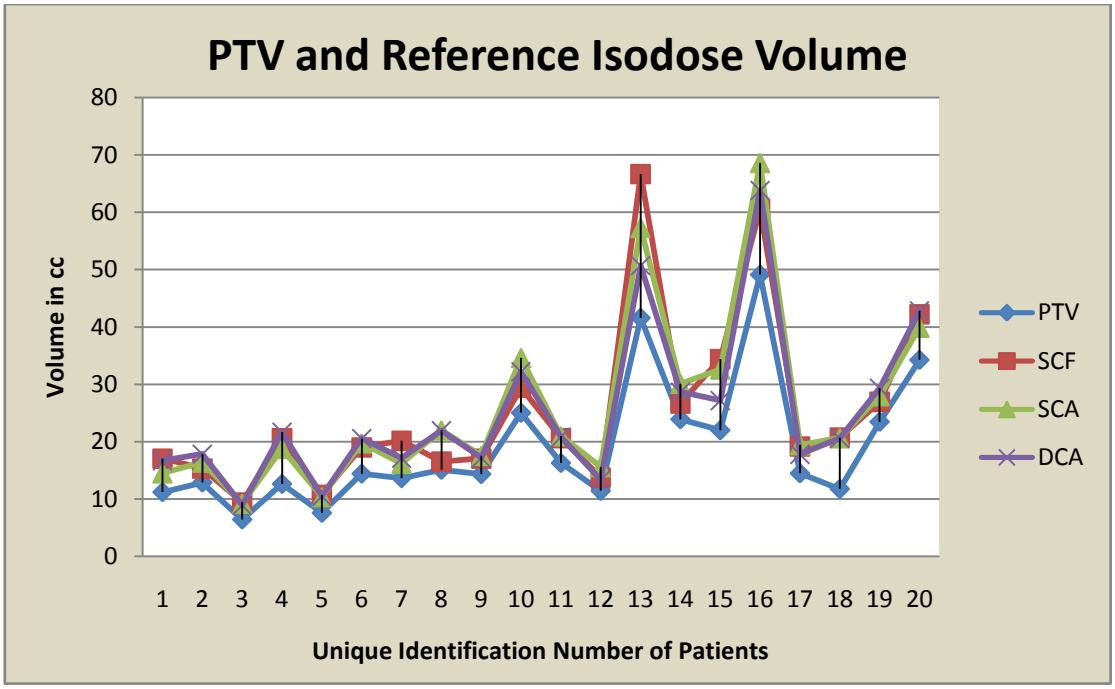



**Fig 5: Reference Isodose Volume with respect to the PTV in all the subjects (PTV= Planning target volume, RIV= Reference isodose volume)**

To assess the correlation between Reference Isodose Volume and PTV, spearman rank correlation (rho) was used. The PTV and RIV value in the techniques SCF, SCA and DCA were positively correlated with rho of 0.84, 0.95 and 0.92 respectively, which is statistically significant with p-value of <0.001( Fig 12).

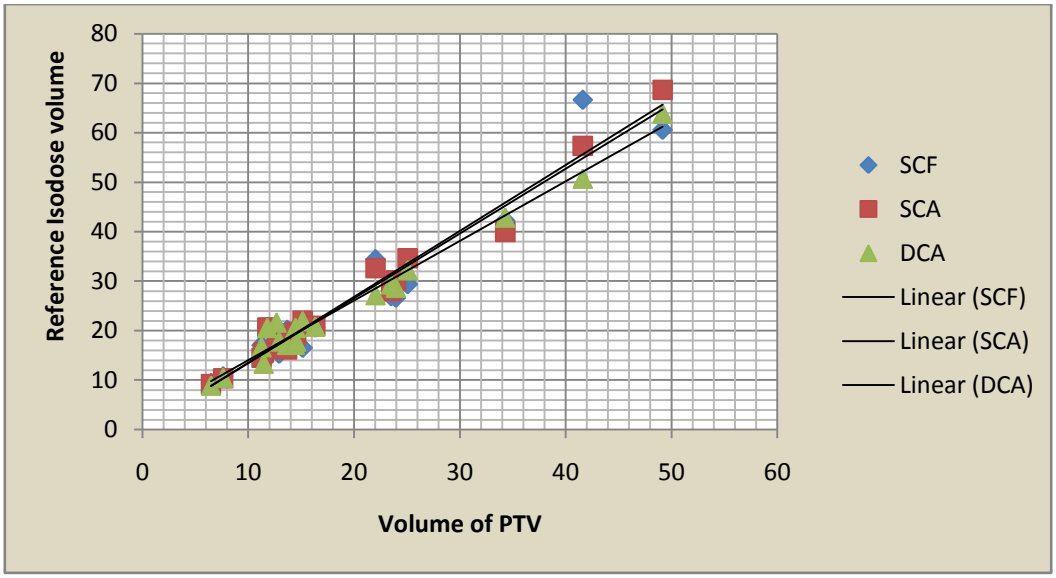



**Fig 6: Correlation of Reference Isodose volumes with PTV**

## 7.4 PTV receiving 95% of the prescribed dose

Mean PTV receiving the 95% of the prescription dose was reported in all the three plans. PTV coverage was adequate for SCF and DCA plans but <95% was covered in SCA plans, however the difference was not statistically significant (p=0.206). One plan in SCF and two plans in SCA were covered with <90% of the prescribed dose as depicted in Table 7.3 and Fig 13.

**Table 7-3 PTV receiving 95% Dose**

| PTV receiving 95% isodose | | | |
|---|---|---|---|
| S No | SCF | SCA | DCA |
| 1 | 96.00 | 96.90 | 97.90 |
| 2 | 98.80 | 97.60 | 99.00 |
| 3 | 96.00 | 96.50 | 94.00 |
| 4 | 95.50 | 91.00 | 99.20 |
| 5 | 95.56 | 96.20 | 92.40 |
| 6 | 94.70 | 93.90 | 96.00 |
| 7 | 99.70 | **89.50** | 93.00 |
| 8 | 94.50 | 96.90 | 97.50 |
| 9 | 97.15 | 96.70 | 95.18 |
| 10 | 94.60 | 94.80 | 93.30 |
| 11 | 95.70 | 92.70 | 91.90 |
| 12 | 90.00 | 97.20 | 96.60 |
| 13 | 95.40 | 96.60 | 96.80 |
| 14 | **89.60** | 95.40 | 95.50 |
| 15 | 95.90 | 95.00 | 98.10 |
| 16 | 95.40 | **88.00** | 95.40 |
| 17 | 97.60 | 95.70 | 98.60 |
| 18 | 96.00 | 93.40 | 91.80 |
| 19 | 95.30 | 90.00 | 94.50 |
| 20 | 94.50 | 91.70 | 95.80 |
| Mean & SD | 95.39 ± 2.35 | 94.29 ± 2.89 | 95.62 ± 2.36 |
| p Value | 0.206 | | |

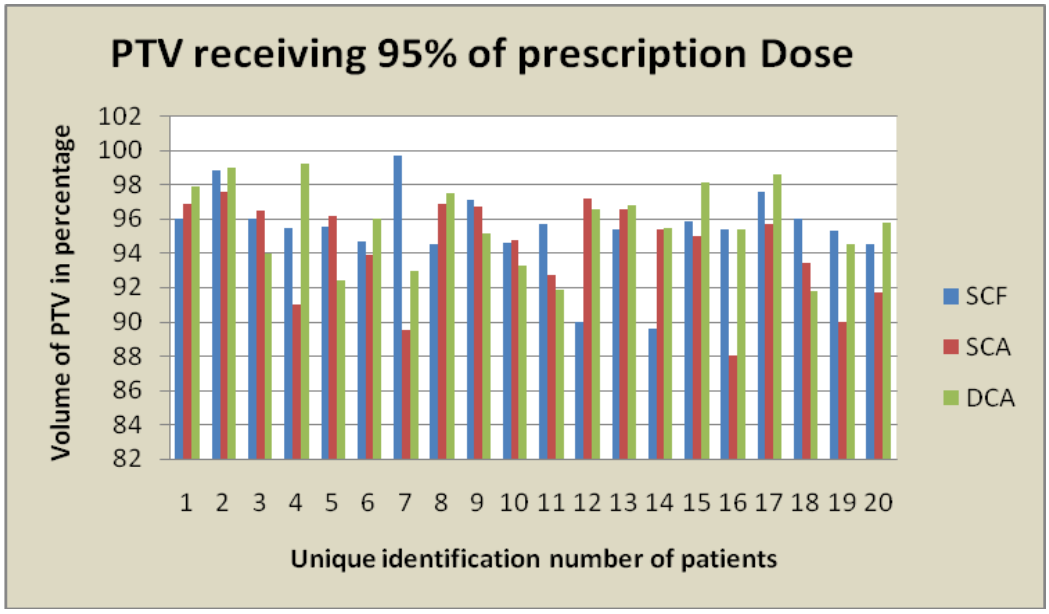



**Fig 7: Mean PTV receiving the 95% isodose in the three SRT plans**

## 7.5 Conformity index

The conformity index was developed to analyse the spatial dose distribution in each section of the target. RTOG defined conformity index as with the formula,

Conformity Index (RTOG) = $\frac{VRI}{TV}$ where VRI reference isodose volume, and TV target volume. Conformity index was calculated for all the three plans for patient data sets.

**Table 7-4 Conformity Index of the three SRT plans**

| Conformity Index | | | |
|---|---|---|---|
| S No | SCF | SCA | DCA |
| 1 | 1.52 | 1.29 | 1.48 |
| 2 | 1.19 | 1.27 | 1.38 |
| 3 | 1.46 | 1.42 | 1.38 |
| 4 | 1.63 | 1.48 | 1.71 |
| 5 | 1.41 | 1.36 | 1.38 |
| 6 | 1.32 | 1.37 | 1.42 |
| 7 | 1.47 | 1.18 | 1.26 |
| 8 | 1.09 | 1.45 | 1.45 |
| 9 | 1.19 | 1.22 | 1.20 |
| 10 | 1.17 | 1.38 | 1.29 |
| 11 | 1.26 | 1.29 | 1.28 |
| 12 | 1.20 | 1.36 | 1.17 |
| 13 | 1.60 | 1.38 | 1.22 |
| 14 | 1.11 | 1.26 | 1.20 |
| 15 | 1.56 | 1.48 | 1.24 |
| 16 | 1.23 | 1.40 | 1.30 |
| 17 | 1.32 | 1.34 | 1.23 |
| 18 | 1.76 | 1.75 | 1.75 |
| 19 | 1.15 | 1.19 | 1.25 |
| 20 | 1.23 | 1.16 | 1.25 |
| Average & SD | 1.34 ± 0.19 | 1.35 ± 0.13 | 1.34 ± 0.16 |
| p Value | 0.951 | | |

*SCF =Static conformal field, SCA=Static conformal arc, DCA=Dynamic conformal arc, SD=Standard deviation*

RTOG conformity index was within acceptable limits (Conformity Index between 1 and 2) for all the techniques across all patient data sets. Mean conformity for SCF, SCA and DCA was 1.34, 1.35 and 1.34 respectively. The difference in the conformity indices among the three plans was not significant (*p* value = 0.951). In SCF plan 75% of the plans were having Conformity index of <1.5, whereas in the case of SCA and DCA plans 95% and 90% had Conformity Index of <1.5 (Table 7.4 and Fig. 14).

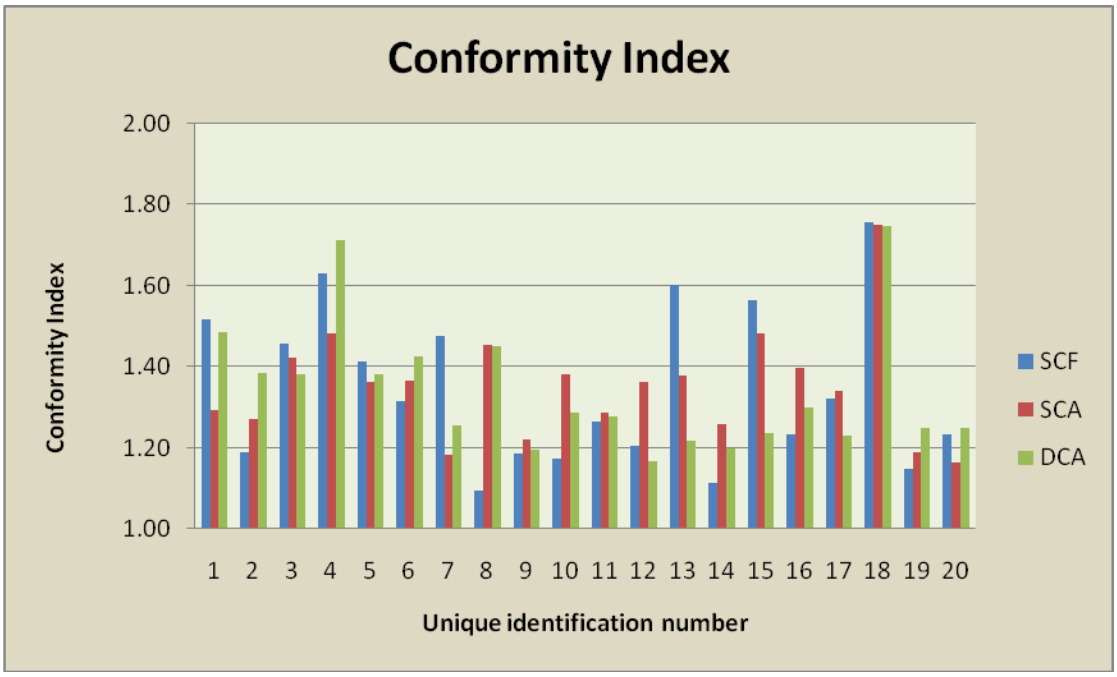



**Fig 8: Conformity Index of 20 patient data sets for the three SRT plans**

## 7.6 Homogeneity index

The homogeneity index represents how the dose is spatially distributed in the target volume. HI was described by the RTOG as, $HI_{RTOG} = \frac{Imax}{RI}$

$I_{max}$ = maximum isodose in the target, and RI = reference isodose.

**Table 7-5 Homogeneity index showing mean and standard deviation in three SRT plans**

| Homogeneity index | | | |
|---|---|---|---|
| S No | SCF | SCA | DCA |
| 1 | 1.07 | 1.07 | 1.07 |
| 2 | 1.06 | 1.07 | 1.07 |
| 3 | 1.08 | 1.06 | 1.06 |
| 4 | 1.06 | 1.03 | 1.08 |
| 5 | 1.06 | 1.09 | 1.08 |
| 6 | 1.06 | 1.09 | 1.07 |
| 7 | 1.06 | 1.08 | 1.07 |
| 8 | 1.07 | 1.07 | 1.06 |
| 9 | 1.06 | 1.08 | 1.08 |
| 10 | 1.07 | 1.09 | 1.08 |
| 11 | 1.07 | 1.08 | 1.07 |
| 12 | 1.07 | 1.05 | 1.07 |
| 13 | 1.07 | 1.07 | 1.08 |
| 14 | 1.08 | 1.08 | 1.07 |
| 15 | 1.06 | 1.07 | 1.06 |
| 16 | 1.06 | 1.11 | 1.08 |
| 17 | 1.06 | 1.10 | 1.08 |
| 18 | 1.08 | 1.08 | 1.11 |
| 19 | 1.08 | 1.10 | 1.09 |
| 20 | 1.08 | 1.12 | 1.08 |
| Average & SD | 1.07 ± 0.01 | 1.08 ± .02 | 1.08 ± .01 |
| p Value | 0.033 | | |

SCF =Static conformal field, SCA=Static conformal arc, DCA=Dynamic conformal arc, SD=Standard deviation

The volume of the Reference Isodose (95% isodose line) was created and measured in cc. Mean homogeneity index was 1.07 ± 0.01, to 1.08 ± 0.02 and 1.08 ± 0.02 in SCF, SCA and DCA plans respectively (*p* value=0.033). In all the plans the homogeneity index was within the RTOG protocol. The minimum homogeneity index was 1.03 and maximum homogeneity was 1.12 across all the plans. In majority of the plans the homogeneity index was <1.10, however four out of 20 plans in SCA and one out of 20 plans in DCA was above 1.10. Homogeneity index is presented in Table 7.5 and Fig 15.

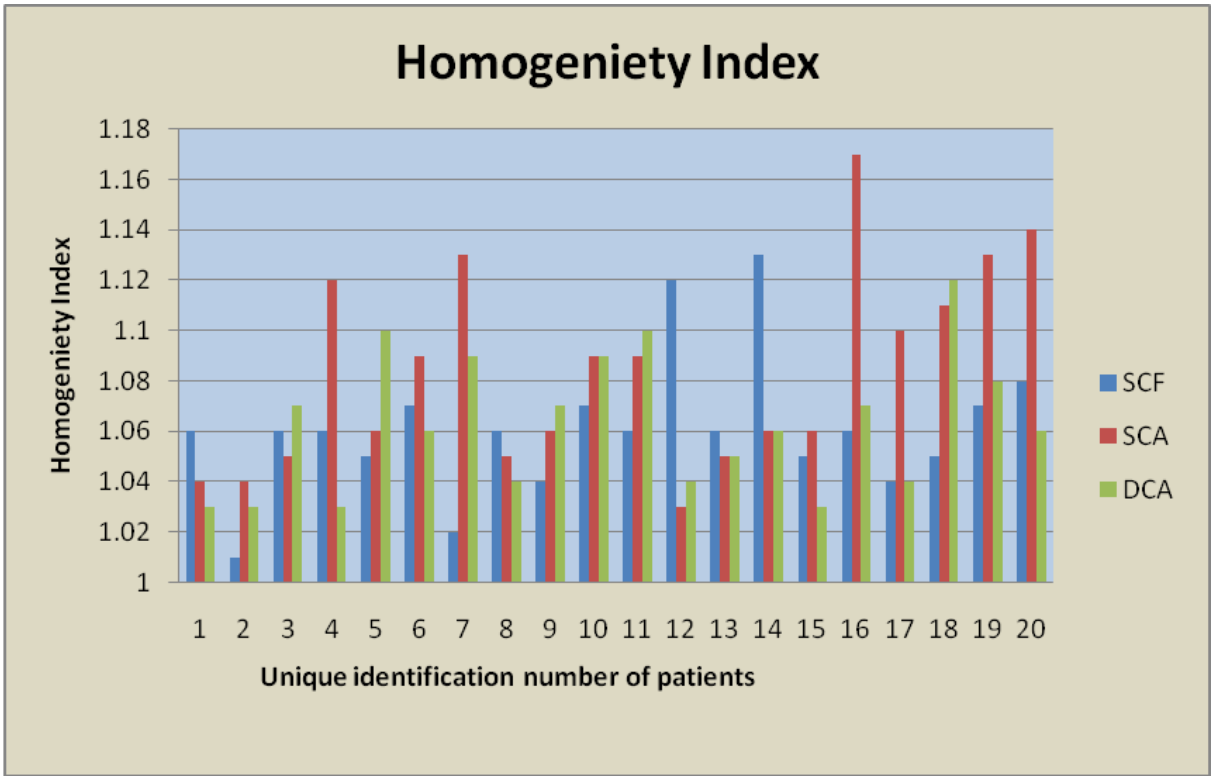



**Fig 9: Homogeneity Indices of all the three plans**

## 7.7 Quality of Coverage

Quality of coverage (RTOG) $= \frac{Imin}{RI}$ where I-min is minimum dose received by the target and RI is the reference isodose.

**Table 7-6 Quality of coverage for all the data sets for three-SRT plans**

| **Quality of Coverage** | | | |
|---|---|---|---|
| S No | SCF | SCA | DCA |
| 1 | 95.05 | **89.89** | 96.11 |
| 2 | 96.00 | 91.37 | 96.42 |
| 3 | 94.84 | **86.00** | 95.58 |
| 4 | **85.05** | **79.89** | 96.95 |
| 5 | 96.84 | **79.26** | 103.78 |
| 6 | 94.21 | **86.21** | 95.47 |
| 7 | 95.47 | **89.79** | 96.22 |
| 8 | 90.00 | 90.53 | 94.21 |
| 9 | 94.84 | 90.53 | 94.42 |
| 10 | 92.63 | **88.74** | 90.40 |
| 11 | 91.68 | 92.42 | 91.37 |
| 12 | 94.83 | 95.89 | 92.32 |
| 13 | **86.84** | 90.32 | 92.53 |
| 14 | **83.26** | 92.95 | 92.74 |
| 15 | 95.37 | **79.89** | 91.27 |
| 16 | 93.16 | **78.95** | **89.58** |
| 17 | 97.05 | **78.53** | 96.63 |
| 18 | **85.68** | **89.26** | **80.32** |
| 19 | 92.74 | **82.95** | 93.37 |
| 20 | **81.76** | **60.18** | **89.58** |
| Average & SD | 91.87 ± 4.7 | 85.68 ± 8.02 | 93.46 ±4.51 |
| p Value | 0.001 | | |

SCF =Static conformal field, SCA=Static conformal arc, DCA=Dynamic conformal arc, SD=Standard deviation

Mean Quality of coverage was within the acceptable limits of RTOG (>90%) in SCF and DCA plans, but for SCA plan quality of coverage had minor deviation (80-89%). The mean quality of coverage was 85.68 ± 8.02 % in SCA plan however it was within the acceptable limit with minor deviation (Fig 4.7). This difference of quality of coverage among the three plans was statistically significant (p <0.001). The quality of coverage showed minor deviation for 5 SCF plans, 7 SCA plans and 3 DCA plans. There was major deviation in 6 SCA plans and no major deviation in SCF and DCA plans (Table 7.6 and Fig 16).

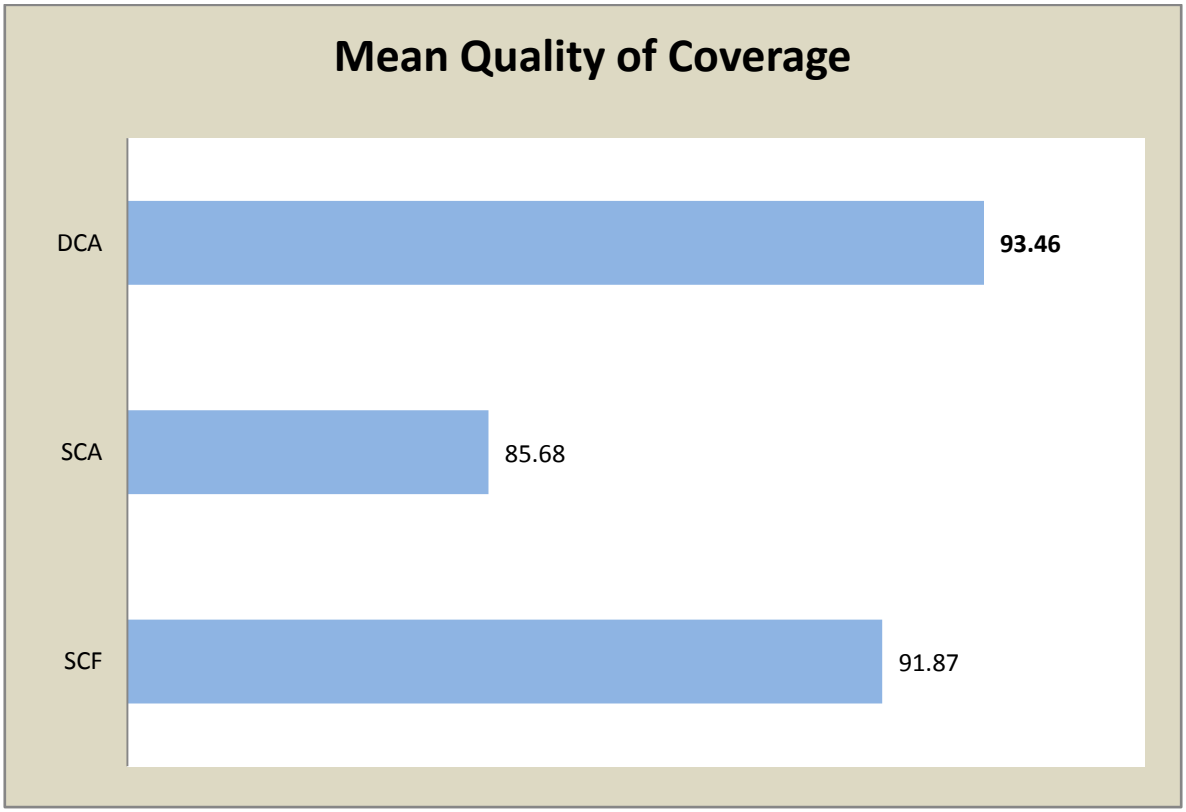



**Fig 10: Mean Quality of target Coverage of the three SRT plans**

*SCF =Static conformal field, SCA=Static conformal arc, DCA=Dynamic conformal arc*

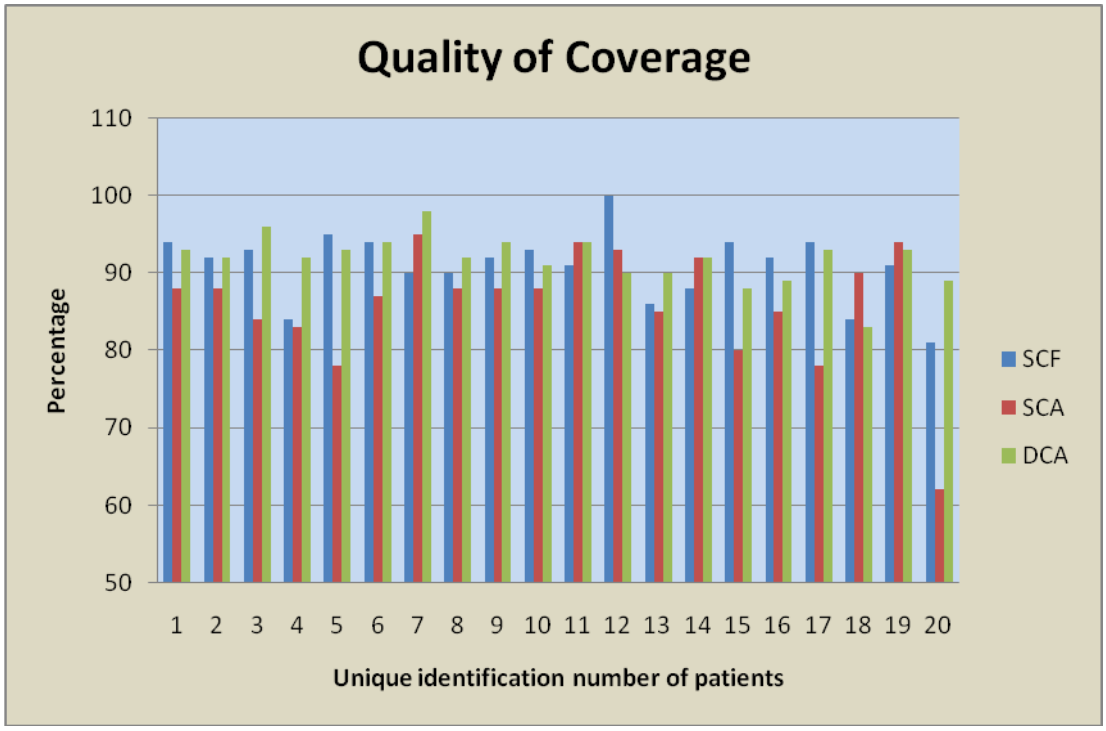



**Fig 11: of coverage in percentage for three SRT techniques**

The association between PTV and Quality of Coverage from the plans SCF, SCA and DCA were negatively correlated with the spearman rank correlation of -0.46, -0.14 and -0.58 respectively (Fig 18). The Quality of Coverage from technique SCF and technique SCA was statistically significant with the p-value of 0.041 and 0.007 respectively.

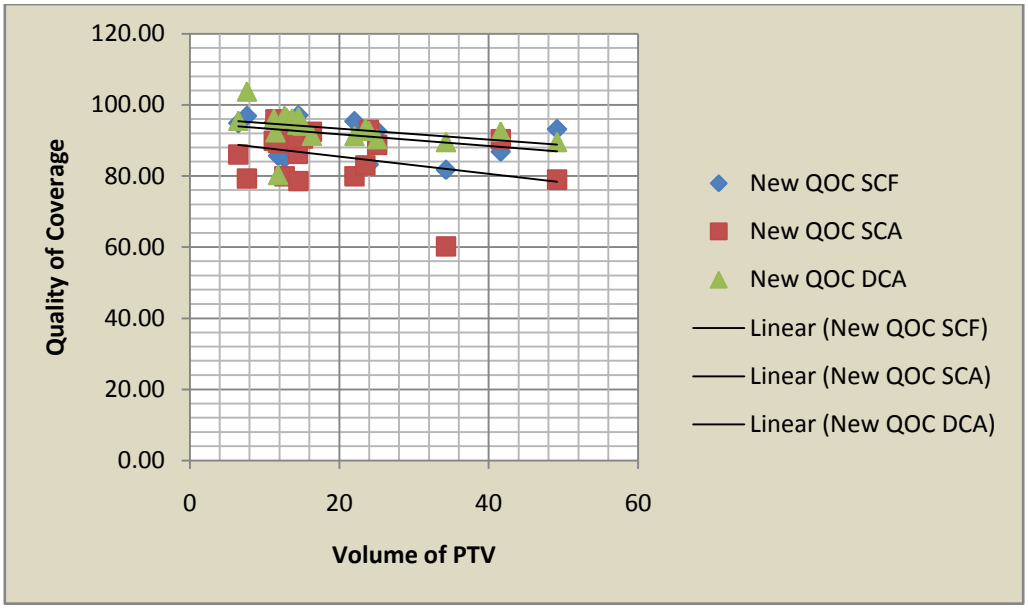



**Fig 12: Correlation of the Quality of coverage with volume of PTV**

**Table 7-7 p values of the three SRT techniques for Conformity Index, Homogeneity Index and Quality of coverage**

| P values | | | |
|---|---|---|---|
| Plans | Conformity Index | Homogeneity Index | Quality of Coverage |
| SCA vs SCF | 0.813 | 0.008 | 0.001 |
| DCA vs SCF | 0.965 | 0.075 | 0.357 |
| DCA vs SCA | 0.779 | 0.335 | 0.001 |

When SCF technique was compared with SCA there was significant statistical difference for the Homogeniety index and Quality of Coverage but not for Conformity Index. There was no statistical significant difference between DCA and SCF plans for Conformity Index, Homogeniety Index and Quality of Coverage parameters/

variables. Comparison between DCA and SCA revealed a statistical difference for Quality of Coverage (Mean quality of coverage was 93.46% in DCA plan and 85.68% in SCA) but not for Conformity and Homogeniety indices (Table 7.7).

## 7.8 Maximum, Minimum and Mean dose in the PTV

The mean maximum dose in the SCF plan was 101.57 ± 0.262, whereas in SCA and DCA plans, the mean maximum dose was higher but it was not statistically significant. The mean minimum dose in the target was lowest in the SCA plan (81.39 ± 4.11) as compared to the SCF and DCA plans which was statistically significant (p=0.002). The average mean dose was about 98% in all the three plans (Table 7.8).

**Table 7-8 the average maximum, minimum and mean dose of the target**

| Doses in the target in percentage | | | | |
|---|---|---|---|---|
| Plan | Measure | Maximum dose | Minimum Dose | Mean Dose |
| SCF | Mean+SD | 101.57 ± 0.26 | 87.27 ± 2.51 | 98.05 ± 0.26 |
| SCA | Mean+SD | 102.45 ± 1.10 | 81.39 ± 4.11 | 98.40± 0.35 |
| DCA | Mean+SD | 102.08 ± 0.34 | 88.78 ± 1.95 | 98.56 ± 0.28 |
| | p-Value | 0.319 | 0.002 | 0.22 |

*SCF =Static conformal field, SCA=Static conformal arc, DCA=Dynamic conformal arc*

## 7.9 Monitor Units for the three SRT plans

All the plans were compared in terms of time required to deliver single fraction. The time for the set up of the patient for in all the three plans assumed to be same. However the difference in the time of treatment delivery may vary depending on the number of monitor units required to deliver the radiation. In this study, monitor units was calculated to deliver single fraction (1.8Gy) in SCF, SCA and DCA techniques for 10 patients' treatment plans (Table 7.9).

**Table 7-9 Monitor Units required for delivering single fraction**

| Monitor Units | | | |
|---|---|---|---|
| S No | SCF | SCA | DCA |
| 1 | 251 | 251 | 249 |
| 2 | 271 | 266 | 268 |
| 3 | 283 | 262 | 262 |
| 4 | 256 | 261 | 257 |
| 5 | 264 | 278 | 279 |
| 6 | 269 | 263 | 259 |
| 7 | 271 | 267 | 268 |
| 8 | 254 | 264 | 259 |
| 9 | 274 | 266 | 268 |
| 10 | 260 | 268 | 255 |
| Average & SD | 265.3 ± 10 | 264.6 ± 6 | 262.4 ± 8 |
| p value | 0.54 | | |

*SCF= Static conformal field, SCA=Static conformal arc, DCA=Dynamic conformal arc and SD= Standard deviation.*

The average monitor units required to deliver the single fraction of radiation did not differ significantly in the three plans. However the monitor units to deliver single fraction of RT is relatively less in the DCA plans, but the difference was not statistically significant (p=0.54). Median values of monitor units were 266.5, 265 and 260.5 in SCF, SCA and DCA plans respectively.

**7.10 DVH Analysis**

The comparison of the isodose lines of one patient data set is shown in the Fig 19. In DCA and SCA plans, lower isodose lines are conformal to the target compared to the SCF plan. The isodose distribution analysis showed that in SCF plan the dose spillage was more on the temporal lobes.

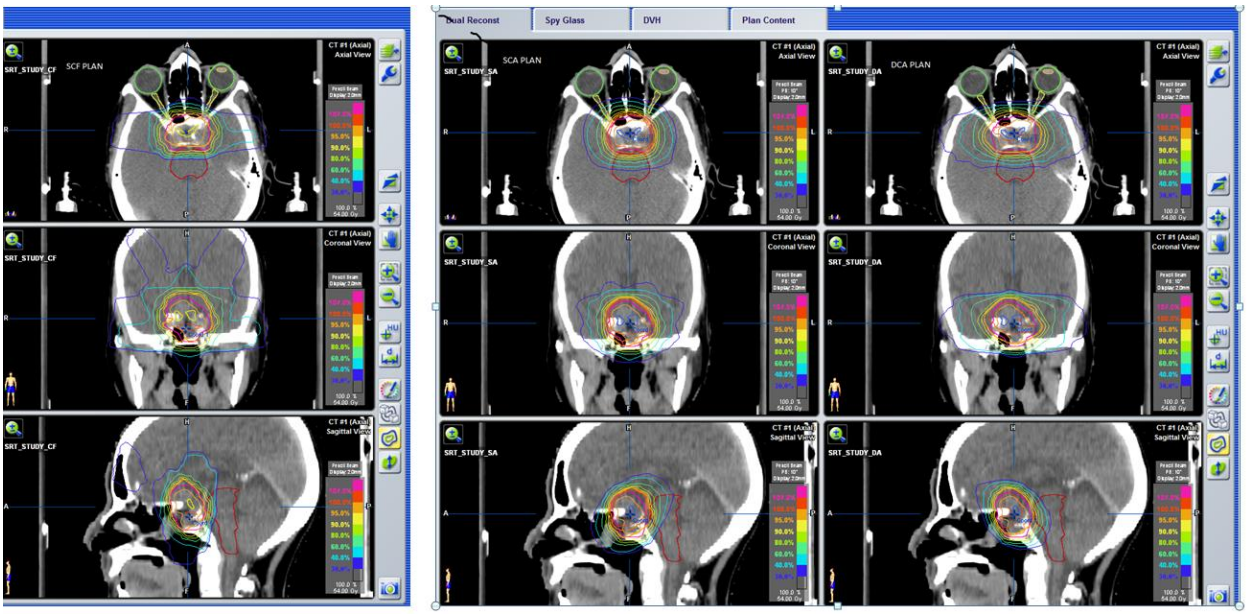



Fig 13 : distribution of one of the patient's plans, left-SCF plan, middle- SCA and right - DCA plan. Blue coloured isodose represents 30% isodose line

## 7.11 Dose to the organs at risk (OAR)

### 7.11.1 Dose to Brain stem

**Table 7-10 dose to brain stem**

| Dose to brain stem | | | |
|---|---|---|---|
| S No | SCF | SCA | DCA |
| 1 | 52.34 | 53.05 | 52.92 |
| 2 | 23.45 | 37.46 | 29.80 |
| 3 | 51.71 | 50.68 | 50.92 |
| 4 | 44.88 | 50.44 | 49.00 |
| 5 | 46.98 | 45.57 | 48.03 |
| 6 | 38.04 | 41.28 | 37.30 |
| 7 | 53.61 | 53.66 | 53.74 |
| 8 | 53.45 | **54.48** | **54.24** |
| 9 | 49.06 | 50.85 | 48.50 |
| 10 | 51.16 | 53.58 | 51.74 |
| 11 | 53.76 | 53.31 | 53.49 |
| 12 | 25.87 | 47.98 | 36.95 |
| 13 | **54.39** | 53.53 | **54.09** |
| 14 | 51.96 | 52.99 | **54.57** |
| 15 | 52.69 | **54.56** | 53.13 |
| 16 | 53.92 | **54.85** | **54.75** |
| 17 | 53.61 | **56.82** | 53.59 |
| 18 | 26.56 | 28.32 | 33.70 |
| 19 | 53.93 | 52.70 | 52.49 |
| 20 | **54.11** | **55.46** | **54.67** |
| Average | 47.274 | 50.0785 | 48.881 |
| Std Dev | ± 10.27 | ±7.04 | ±7.79 |
| p value | 0.019 | | |

The maximum point dose to brain stem ranged from 23.45Gy to 54.39Gy in SCF, 28.32Gy to 56.82Gy in SCA and 29.8Gy to 54.75Gy in DCA plan. SCF technique delivered the minimum dose to the brain stem with 2 plans exceeding 54Gy while in SCA and DCA 5 each exceeded 54Gy. Highest dose to brain stem, 56.82 Gy was found in one of the SCA plans (Table 7.10, Fig 20 and 21). The average dose to brain stem was minimal in SCF plans and it was statistically significant (p= 0.019).

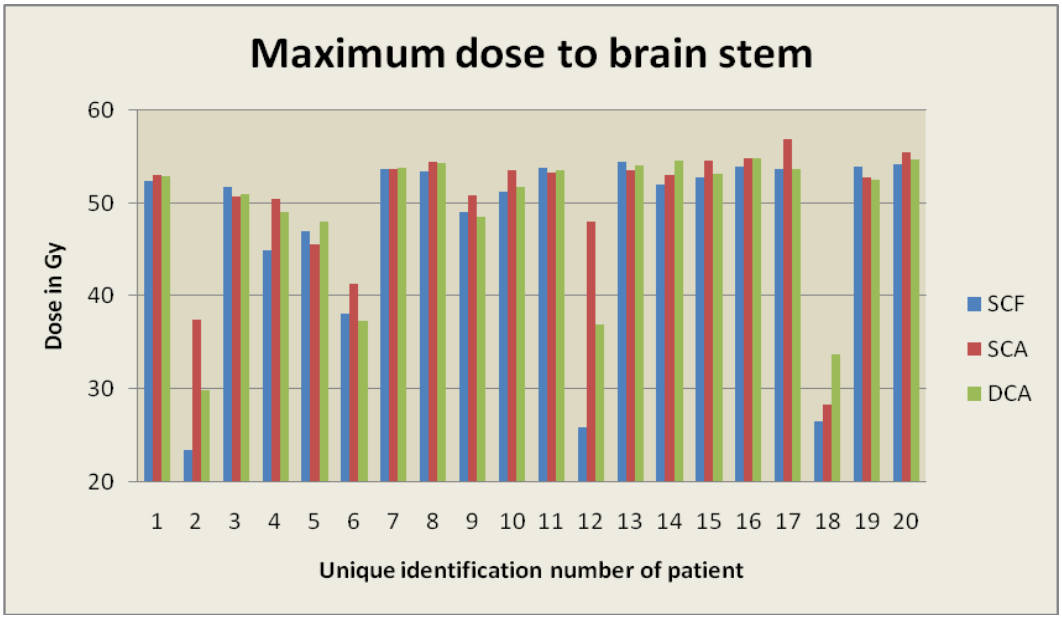



**Fig 14: maximum point dose to brain stem of three SRT plans**

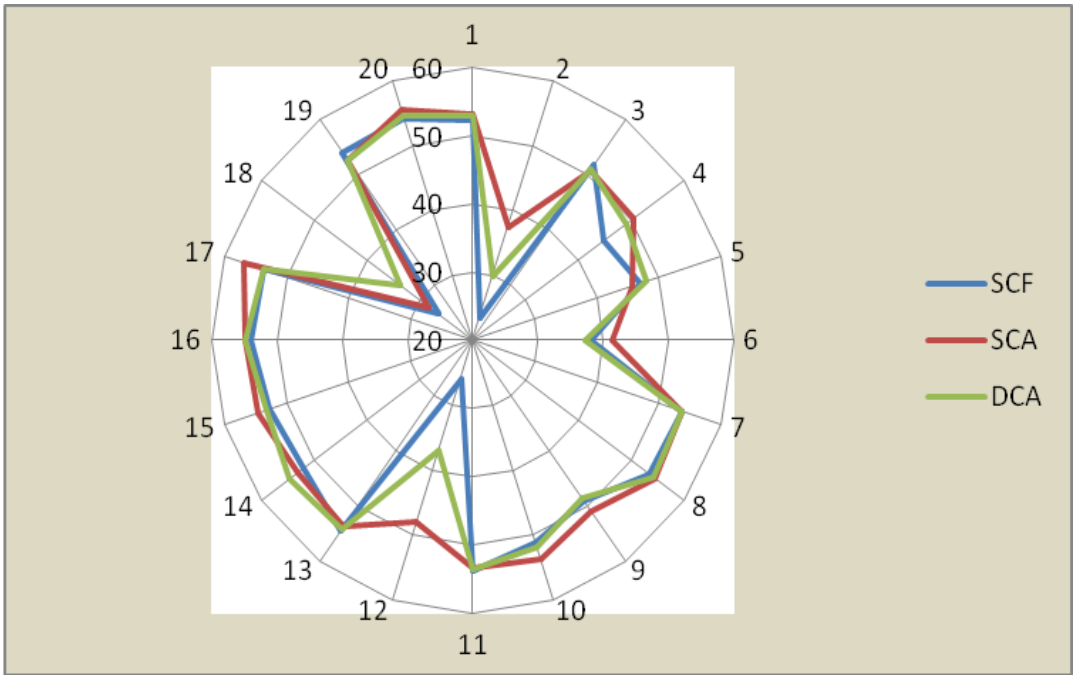



**Fig 15: Radar diagram showing the maximum dose to the brain stem from 20Gy to 60Gy in three techniques of SRT for 20 patients' data sets**

### 7.11.2 Dose to Optic chiasm

Most of the patient data sets had optic chiasm was inside the target volume or closely associated with target volume.

**Table 7-11 Maximum dose to the optic chiasm in the three SRT plans**

| Dose to Optic chiasm | | | |
|---|---|---|---|
| S No | SCF | SCA | DCA |
| 1 | **54.81** | **54.62** | **54.67** |
| 2 | 53.35 | **54.40** | **54.88** |
| 3 | 53.58 | **54.59** | **54.44** |
| 4 | 53.25 | 53.16 | 53.06 |
| 5 | 53.55 | 53.84 | **54.35** |
| 6 | **54.38** | **54.94** | **54.56** |
| 7 | **54.22** | 53.82 | 53.87 |
| 8 | 53.61 | **54.88** | **54.50** |
| 9 | 53.45 | 53.78 | 53.88 |
| 10 | 53.57 | **55.50** | **54.60** |
| 11 | **54.12** | **54.83** | **54.42** |
| 12 | **54.53** | **54.56** | **54.57** |
| 13 | 53.62 | **54.46** | **54.03** |
| 14 | **54.00** | **54.46** | 52.71 |
| 15 | 53.47 | **54.56** | 53.96 |
| 16 | 52.99 | **54.61** | 53.96 |
| 17 | 53.85 | **55.51** | **54.23** |
| 18 | **54.37** | **54.83** | **55.69** |
| 19 | 53.64 | 53.73 | **54.04** |
| 20 | 53.10 | **54.96** | **54.18** |
| Average | 53.77 | 54.50 | 54.23 |
| SD | ± 0.49 | ±0.59 | ±0.62 |
| p value | 0.001 | | |

*CF =Static conformal field, SCA=Static conformal arc, DCA=Dynamic conformal arc*

The maximum point dose received by optic chiasm ranged from 52.99 to 54.81Gy in SCF, 53.16 to 55.51Gy in SCA and 52.59 to 55.69Gy in DCA plans. Static conformal field (SCF) plan delivered the least dose to optic chiasm compared to SCA and DCA plans. None of the plans exceeded 55Gy to optic chiasm in SCF plans, whereas two plans in SCA and one plan in DCA plan (Table 7.11, Fig 22 and 23). The $d_{max}$ exceeded > 54Gy in 7/20, 15/20 and 14/20 in SCF, SCA and DCA plans respectively. Dose to optic chiasm is represented in radar diagram in Fig 22.

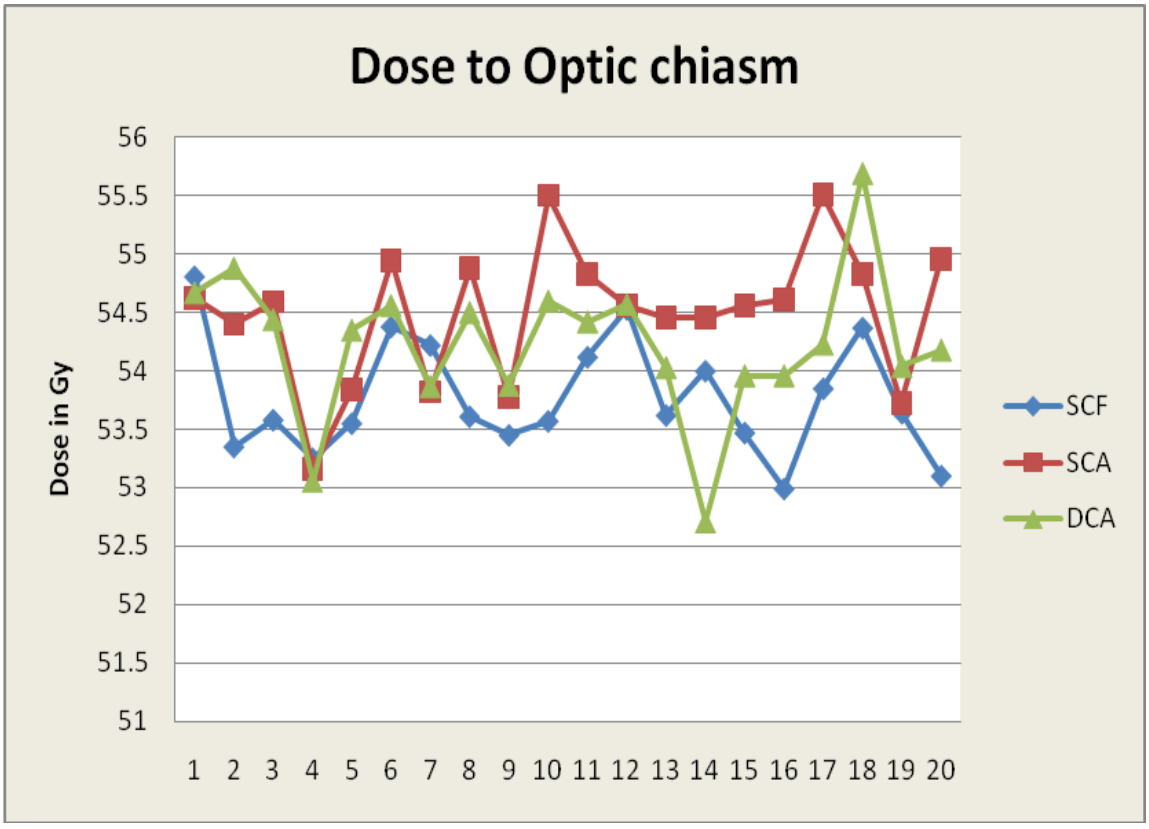



**Fig 16: The maximum dose to the optic chiasm in three SRT plans**

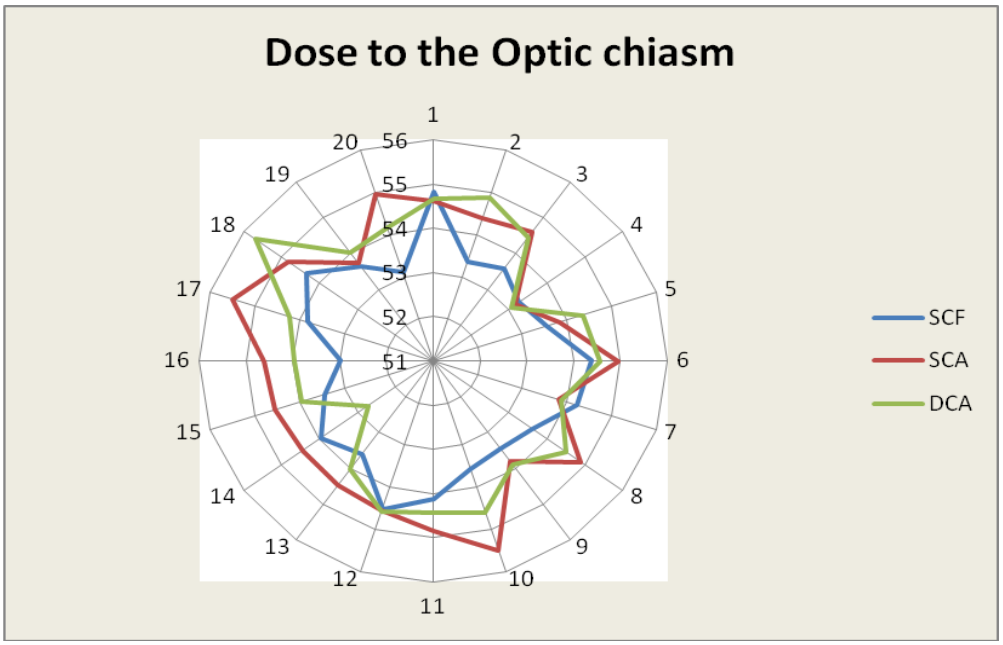



**Fig 17: The radar diagram showing dose to the optic chiasm in 20 data sets for three SRT plans (SCF, SCA and DCA)**

### 7.11.3 Dose to Optic nerves

The maximum dose to left optic nerve ranged from 2.96Gy to 51.77Gy, 7.15Gy to 52.06Gy and 4.36Gy to 52.09Gy in SCF, SCA and DCA plans respectively. Mean doses with standard deviation are presented in Table 7.12 (p value= 0.559). The maximum doses to right optic nerve ranged from 5.72Gy to 51.35Gy, 8.88Gy to 52.84Gy and 7.55Gy to 52.65Gy in SCF, SCA and DCA plans respectively. The mean values are presented in Table 7.12 with standard deviation (p=0.001).

**Table 7-12 Maximum doses to the left and right optic nerves with mean, standard deviation and p values**

| Dose to left optic nerve | | | | Dose to right optic nerve | | |
|---|---|---|---|---|---|---|
| S No | SCF | SCA | DCA | SCF | SCA | DCA |
| 1 | 20.67 | 22.23 | 28.87 | 35.40 | 35.40 | 36.14 |
| 2 | 17.37 | 23.69 | 22.67 | 14.98 | 23.05 | 20.44 |
| 3 | 32.39 | 21.79 | 26.67 | 50.35 | 50.06 | 51.04 |
| 4 | 19.42 | 23.22 | 26.49 | 7.05 | 28.46 | 24.42 |
| 5 | 28.35 | 12.32 | 13.21 | 41.26 | 37.59 | 46.89 |
| 6 | 51.77 | 52.06 | 52.49 | 51.35 | 52.84 | 52.65 |
| 7 | 26.11 | 25.77 | 22.17 | 21.85 | 25.59 | 22.98 |
| 8 | 2.96 | 7.15 | 4.36 | 9.22 | 22.10 | 23.62 |
| 9 | 16.73 | 17.9 | 20.30 | 13.75 | 21.52 | 20.66 |
| 10 | 49.86 | 49.7 | 51.00 | 49.59 | 51.98 | 52.69 |
| 11 | 27.27 | 33.34 | 32.73 | 24.07 | 30.33 | 30.26 |
| 12 | 36.90 | 40.42 | 34.14 | 26.10 | 36.00 | 27.96 |
| 13 | 32.58 | 25.05 | 30.30 | 28.59 | 28.62 | 30.39 |
| 14 | 31.00 | 32.57 | 33.18 | 44.03 | 45.77 | 46.32 |
| 15 | 44.87 | 37.53 | 43.36 | 49.55 | 51.45 | 49.19 |
| 16 | 49.90 | 40.86 | 47.62 | 50.42 | 47.63 | 50.82 |
| 17 | 28.94 | 25.25 | 25.21 | 49.08 | 45.11 | 45.94 |
| 18 | 15.33 | 31.75 | 29.17 | 19.02 | 23.65 | 23.96 |
| 19 | 5.04 | 8.54 | 8.05 | 5.72 | 8.88 | 7.55 |
| 20 | 17.84 | 20.39 | 26.16 | 18.32 | 18.66 | 27.88 |
| Average | 27.77 | 27.58 | 28.91 | 30.49 | 34.23 | 34.59 |
| Std Dev | 14.00 | 12.30 | 12.86 | 16.51 | 13.06 | 13.66 |
| p value | 0.559 | | | 0.001 | | |

*SCF =Static conformal field, SCA=Static conformal arc, DCA=Dynamic conformal arc*

## 7.12 Volume of Brain Receiving 5Gy, 6Gy, 10Gy, 20Gy and 40Gy

In this study we have collected data on volume of the brain receiving low (5Gy, 6Gy) medium (10Gy and 20Gy) and high dose (40Gy). The data on mean doses with standard deviation for brain volume receiving 5Gy is presented in Table 7.13

**Table 7-13 Volume of brain in cc receiving the 5Gy dose in three SRT techniques**

| Volume of brain in cc receiving 5Gy | | | |
|---|---|---|---|
| S No | SCF | SCA | DCA |
| 1 | 270 | 342 | 339 |
| 2 | 410 | 506 | 525 |
| 3 | 293 | 308 | 297 |
| 4 | 381 | 526 | 543 |
| 5 | 343 | 379 | 433 |
| 6 | 446 | 552 | 418 |
| 7 | 342 | 516 | 517 |
| 8 | 389 | 484 | 444 |
| 9 | 410 | 544 | 610 |
| 10 | 446 | 752 | 493 |
| 11 | 471 | 576 | 531 |
| 12 | 326 | 447 | 514 |
| 13 | 582 | 1067 | 1025 |
| 14 | 595 | 623 | 588 |
| 15 | 456 | 692 | 672 |
| 16 | 714 | 813 | 764 |
| 17 | 313 | 262 | 560 |
| 18 | 347 | 586 | 613 |
| 19 | 539 | 717 | 676 |
| 20 | 590 | 701 | 806 |
| Average volume in cc | 433.15 | 569.65 | 568.4 |
| Std Dev | ± 118.5 | ± 180.24 | ± 162.8 |
| p value | 0.001 | | |

Mean volume with Standard deviation of the brain receiving the 5Gy is 433.15 ± 118.5 cc, 569.65 ± 180.24cc and 568.4 ± 162.8cc in SCF, SCA and DCA plans

respectively. The V5 Brain was the lowest in SCF plans compared to the other two plans SCA and DCA and it was statistically significant (p= <0.001).

Mean dose of the V6 Brain, V10 Brain, V20 Brain and V40 Brain is presented in the Table 7.14 with standard deviation and p values for the three plans. The mean volume of the brain receiving 5 and 6Gy were lower in SCF technique compared to SCA and DCA techniques, whereas higher volume of brain receiving 10Gy (V10), 20Gy (V20) and 40 Gy (V40) was found in SCF technique as compared to SCA and DCA techniques. The volume of brain receiving 5, 6, 10, 20 and 40Gy doses were comparable in SCA and DCA techniques.

**Table 7-14 Mean volume of the brain in cc receiving 5Gy, 6Gy, 10Gy, 20Gy and 40Gy**

| | DOSE TO THE VOLUME OF BRAIN RECEIVING 5 Gy | | |
|---|---|---|---|
| Plan | Mean dose | Std deviation | P value |
| SCF | 433.15 | 118.50 | |
| SCA | 566.25 | 180.24 | 0.001 |
| DCA | 567.00 | 162.80 | |
| | DOSE TO THE VOLUME OF BRAIN RECEIVING 6 Gy | | |
| Plan | Mean dose | Std deviation | P value |
| SCF | 419.95 | 116.83 | |
| SCA | 479.10 | 177.80 | 0.016 |
| DCA | 476.35 | 163.30 | |
| | DOSE TO THE VOLUME OF BRAIN RECEIVING 10 Gy | | |
| Plan | Mean dose | Std deviation | P value |
| SCF | 363.95 | 118.29 | |
| SCA | 269.25 | 121.90 | 0.001 |
| DCA | 267.90 | 124.20 | |

| | DOSE TO THE VOLUME OF BRAIN RECEIVING 20 Gy | | |
|---|---|---|---|
| Plan | Mean dose | Std deviation | P value |
| SCF | 143.35 | 103.00 | |
| SCA | 115.55 | 72.78 | 0.0008 |
| DCA | 113.30 | 69.85 | |
| | DOSE TO THE VOLUME OF BRAIN RECEIVING 40 Gy | | |
| Plan | Mean dose | Std deviation | P value |
| SCF | 143.35 | 103.00 | |
| SCA | 115.55 | 72.78 | 0.0008 |
| DCA | 113.30 | 69.85 | |

## 7.13 Treatment Time

The time taken for treatment delivery was measured for all the three techniques for one patient plan for single fraction of radiation (1.8Gy). The measurement was done using water phantom on the machine and time was calculated from starting of the treatment till completion. The time required for set up of the patient has been assumed to be constant.

In SCF plan, the time taken for single fraction radiation delivery from starting of radiation till completion was seven minutes and 40 seconds, whereas time for both SCA and DCA plans was similar 8 minutes 20 seconds (difference of 40 seconds was found). Though the dose rate was set at 600 MU in all the plans, we found that SCA and DCA plans were delivered with dose rate of 136 MU for SCA and DCA techniques and 590 MU per minute for SCF plans.

# DISCUSSION

## 8 Discussion

Pituitary adenoma and Craniopharyngioma are benign tumours, anatomically located over the sellar region and are closely associated with optic apparatus anteriorly and brainstem posteriorly. Stereotactic fractionated radiotherapy delivers highly precise and accurate radiation resulting in reduction in the dose to the organs at risk. SRT has been reported as safe and effective in treating Pituitary adenoma and Craniopharyngioma. Various Linear accelerator based SRT techniques have been defined in the literature (3,4,17).

It's necessary to compare techniques in order to find the best possible technique of SRT for tumours like Pituitary adenoma and Craniopharyngioma, as these tumours are benign and patients survive longer. The techniques were compared in terms of dose conformity and homogeneity within the target and quality of target coverage. The advantages of each technique is analysed in reducing radiation dose to surrounding normal organs at risk. Comparison of volume of the brain receiving low dose of 5Gy and 6Gy corresponding to radiation induced second malignancy, medium and high dose (10, 20, 40Gy) which may impair the cognitive functions (76) were analysed across all the plans of patient data sets.

In this study, dosimetric comparison of the three Linear accelerator based stereotactic radiotherapy (SRT) techniques, Static Conformal Field (SCF), Static Conformal Arc (SCA) and Dynamic Conformal Arc (DCA) for Pituitary adenoma and

Craniopharyngioma was conducted on 20 patient data sets. The reference isodose volume concurs well with PTV in all the three techniques.

## 8.1 Conformity index

Conformity index estimates the dose conformity to the target and also indirectly estimates the dose to the surrounding normal organs. In this study, the conformity index for all the data sets in three techniques was <2 accepting the RTOG criteria, without any violation of the protocols. The mean conformity indices were slightly better in SCF 1.34 (±0.19) and DCA 1.34 (±0.16) than in SCA technique 1.35 (±0.13), but this was not statistically significant ($p$ =0.720).

Similar study was performed by Ammer *et al.*,(77) evaluated the peripheral dose and conformity index for three SRT techniques for the intracranial targets for ten patients, found mean conformity index of 1.34 (±0.13) for Arcs and 1.4 (±0.09) for Conformal fields. The results are similar in the present study.

In case of SCF the angle of the beam or gantry is manually modified or use of field in field approach gives more conformal dose distribution. Similar degree of freedom however in case of Arcs may not be possible for individual fields and it depends on number and length and distance between each arcs used. The change in the shape of MLCs for every 10 degree gantry rotation would probably support the slightly better conformity in DCA plan in the present study.

Dosimetric comparison of the stereotactic radiotherapy techniques with IMRT plans for the 4 simulated targets of the cranial tumors by S D Sharma *et al.*,(50) showed that conformity index was better in SCF (mean CI= 0.71) and in DCA (mean CI=0.72) plans than in SCA plans (mean CI of 0.67). Solberg TD *et al.*, (46) compared dynamic arc radiosurgery (SRS) with static field conformal and noncoplanar circular arcs on a simulated targets of three overlapping spheres and found that the DCA plan was better in dose conformity.

McCollough *et al.*,(17) found that conformal shaped fields using 7-11 beams resulted in the similar dose distribution as single isocentre circular arc technique. They also noted that, the adjacent normal structures can be easily shielded using conformal technique. However the peripheral dose distribution was higher for 7-11 field plans than for the circular fields. They also opined that the dynamic MLC would make an advantage in reducing the peripheral dose.

Study by Wiggenraad *et al.*,(8) comparing IMRT with Dynamic Conformal Arc technique for intracranial tumours, reported a mean conformity index ranging from 1.14 to 1.38 for DCA technique, which is similar to our study. In this study the CI for SCF, SCA and DCA plans were comparable, but SCA was slightly inferior numerically but it was not statistically significant.

## 8.2 Homogeneity index

Mean homogeneity index was 1.07 (±0.01), to 1.08 (±0.02) and 1.08 (±0.02) in SCF, SCA and DCA plans respectively ($p$=0.033). In all the plans the homogeneity index

was within the RTOG protocol. The homogeneity index was comparatively better in the SCF technique.

Cardinale *et al.*,(45)compared three linac based stereotactic radiotherapy techniques for three intracranial test targets having ellipsoid, hemisphere and irregular target and found that CI and HI were higher in arc technique compared to 3D conformal technique. But in our study, we found that there was no significant difference in CI and HI among the three techniques.

Study by Wiggenraad *et al.*(8) comparing IMRT with Dynamic Conformal Arc technique for intracranial tumours, reported a mean homogeneity index ranging from 1.15 to 1.306 for DCA techniques, concluding that DCA technique is more preferred for intracranial targets irrespective of shape and size of the targets.

### 8.3 Quality of target coverage

Mean Quality of coverage was within the acceptable limits of RTOG (>90%) in SCF and DCA plans, but for SCA plan quality of coverage had minor deviation (80-89%). The mean quality of coverage was 85.68% in the case of SCA plan, however it was within the acceptable limit with minor deviation (Fig 16). This difference of quality of coverage among the three plans was statistically significant ($p$ <0.001). The quality of coverage showed minor deviation for 5 SCF plans, 7 SCA plans and 3 DCA plans. There was major deviation in 6 SCA plans and no major deviation in SCF and DCA plans (Table 7.6). There was no significant correlation between the volume of the PTV and quality of coverage.

Wiggenraad *et al.*,(8) compared IMRT with Dynamic Conformal Arc technique for intracranial tumours of different type, shape and size and reported a mean target coverage of 99.1% for DCA technique, which is slightly more than our study 93.46 (±4.51). In the above study, all intracranial tumors irrespective of their location were included. The present study included only sellar and suprasellar tumors which are in close association with critical structures such as optic chiasm and brain stem. Getting optimal target coverage with adequate sparing of these OARs was a challenge in the present study. Comparison of the plans individually for CI, HI and Quality of target coverage favoured the DCA technique (Table 7.7). When SCF technique was compared with SCA there was statistically significant difference for the Homogeniety index and Quality of Coverage but not for Conformity Index. There was no statistically significant difference between DCA, SCA and SCF plans for all the three Conformity, Homogeniety indices and Quality of Coverage. Comparison between DCA and SCA revealed a statistical difference for quality of coverage (Mean quality of coverage was 93.46% in DCA plan and 85.68% in SCA) but not for Conformity and Homogeniety indices. Overall, the results were in favour of DCA technique.

## 8.4 Dose to organs at risk

### 8.4.1 Brainstem and Optic Chiasm

The average $d_{max}$ to brainstem was 47.27Gy, 50.07Gy and 48.88Gy in SCF, SCA and DCA plans respectively (p=0.019). SCF plan was efficient in achieving the dose constraint consistently for 18/20 patients, where as DCA and SCA plans were able to achieve the dose constraint in 15/20 patients. The dose to brain stem was better

controlled in SCF technique because individual selection of beams minimising the entry and exit dose to brain stem was possible.

The maximum dose to the optic chiasm ranged from 52.99 to 54.81Gy in SCF, 53.16 to 55.69Gy in SCA and 52.59 to 55.71Gy in DCA plans. Static conformal field plan was more efficient in reducing the dose to the optic chiasm as compared to the other plans due to the better beam selection as stated above. Wiggenraad *et al.*,(8) in the study comparing IMRT with DCA for intracranial tumours, expressed that sparing the optic system is a challenge when the target is close to it and said that the dose up to 56Gy is acceptable with standard fractionation. None of the patients SRT plan exceeded >55Gy in the present study.

The doses to the optic nerves were well below the constraints in all the cases, none of the plans had optic nerve dose >54Gy. Again SCF was better in sparing the optic nerves than both the arc techniques.

### 8.4.2 Dose to the Brain (V5, V6), (V10, V20) & (V40)

In this study the volume of the brain receiving the lower dose of 5Gy & 6Gy, Intermediate dose of 10Gy & 20Gy and high dose of 40Gy were studied. In both arc techniques DCA and SCA, the volume of the brain receiving the low dose (5Gy and 6Gy) were high compared to the SCF technique which was statistically significant (5Gy p=0.001) (6Gy p=0.016). This is explained from the techniques of arc therapy in which number of fields will be higher (30-40 depending on the number and length of

arc). The small dose from each of these fields is converging to the target resulting in high volume of brain receiving low dose.

Hamilton *et al.*,(49) compared the SCF technique with arc therapy in multiple intracranial targets, and found that the volume of the normal tissue receiving the lower doses (10% of prescription dose) increases with number of fields in the SCF technique and multiple arc technique, the difference was around 1.6 times more in arc technique compared to static fields. Also they have reported volume of the normal tissue receiving high dose (> 90% of the prescribed dose) was similar in arc and static fields using 8-12 fields. Marked difference between volume of the brain receiving the high dose and low dose was not found when the number of fields in static conformal technique is increased beyond 8. In this study it was found that large volume of brain received the low dose (5 and 6Gy) in the arc plans (SCA & DCA) compared to SCF plan which was similar to the observation by Hamilton *et al.*, In the present study, it was also found that the volume of brain receiving intermediate (10, 20) and high dose (40Gy) was higher in SCF plan, with statistical significance (V10 p= 0.001, V20 p=0.008 and V40 p=0.008) compared to arc plans.

### 8.5 Treatment time

In this study, treatment time was calculated for all the three techniques for one patient and the monitor units required to deliver single fraction of radiation was compared for the three plans. The median monitor units required to deliver single fraction RT were 266.5, 265 and 260.5 for SCF, SCA and DCA techniques respectively. Time required

in completing single fraction RT was lesser (7 minutes 40 seconds) in SCF plan compared to SCA and DCA techniques (8 minute 40 seconds). The numbers of fields in SCF were six in this study, and arcs were 4 in both SCA and DCA.

Similar study on monitor units was performed by Solberg *et al.*,(78) in a dosimetric comparative study of static arc, conformal static fields with dynamic arc radiosurgery, in which they found that to achieve more desired dose distributions number of fields required in SCF will increase and may consume more time compared to arc techniques. They have concluded that use of dynamic arc technique is simple to plan and treat.

The difference in the treatment time between the SCF and Arc techniques may be explained based on the dose rate (output in the machine). Dose rate was higher 590MU per minute in SCF technique as compared to SCA and DCA techniques (136MU per minute).

# CONCLUSIONS

## 9 Conclusions

The Linac based stereotactic radiotherapy techniques Static Conformal Field (SCF); Static Conformal Arc (SCA) and Dynamic Conformal arc (DCA) techniques are efficient in delivering highly conformal and homogenous dose to the target in Pituitary adenoma and Craniopharyngioma. The Conformity Index and Homogenity Index were comparable across the three plans but Quality of target coverage was superior in DCA.

Dynamic Conformal Arc (DCA) technique was the best technique among the three in achieving all the indices.

Doses to normal organs, Optic Chiasm and Brain stem were better controlled in SCF technique than SCA and DCA technique.

The volume of the brain receiving 5Gy, 6Gy (low dose) was high in Arc Techniques (SCA & DCA) than in SCF technique. The volume of the brain receiving intermediate (10Gy and 20 Gy) and high doses (40Gy) were higher in SCF techniques than Arc techniques (SCA and DCA).

Significant difference was not found between the techniques in terms of treatment time.

Further research is needed to show clinical benefit of these dosimetric differences.

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**Data Record sheet for the study on Dosimetric analysis of the three SRT techniques, Static conformal field (SCF), Static Conformal Arc (SCA) & Dynamic Conformal Arc (DCA).**

| | | |
|---|---|---|
| 1) | Hospital Number: | |
| 2) | Unique identifying number: | |
| 3) | Age: | |
| 4) | Gender | |
| 5) | Diagnosis | |
| 6) | Prescribed dose of radiation | |
| 7) | Number of fractions of radiation | |
| 8) | Dose per each fraction | |
| 9) | Immobilization devise used | |
| 10) | Dose constraints: | |
| 11) | Dose to Chiasm | |
| 12) | Dose to brain stem | |
| 13) | Dose to left lens | |
| 14) | Dose to right lens | |
| 15) | Dose to left optic nerve | |
| 16) | Dose to right optic nerve | |
| 17) | Reference isodose | |

| SN | Variables | SCF | SCA | DCA |
|---|---|---|---|---|
| 18 | Reference isodose volume | | | |
| 19 | PTV Volume | | | |
| 20 | TV (Tumour volume) | | | |
| 21 | PTV receiving 95% Prescribed dose | | | |
| 22 | Maximum dose (dose maximum) | | | |
| 23 | Maximum dose in Percentage | | | |
| 24 | Minimum dose | | | |
| 25 | Minimum dose in Percentage | | | |
| 26 | Mean dose | | | |
| 27 | Mean dose in Percentage | | | |
| 28 | Conformity index (Conf Index) | | | |
| 29 | Homogeneity index | | | |
| 30 | Quality of coverage | | | |

| | | | | |
|---|---|---|---|---|
| 31 | D5 (Min dose in 5% of PTV) | | | |
| 32 | D95 (Min dose in 95% of PTV) | | | |
| 33 | Maximum Dose to Left Eye | | | |
| 34 | Maximum Dose to Right Eye | | | |
| 35 | Maximum Dose to Brain stem | | | |
| 36 | Maximum Dose to chiasm | | | |
| 37 | Maximum Dose to Left Optic Nerve | | | |
| 38 | Maximum Dose to Right Optic Nerve | | | |
| 39 | Maximum Dose to Left Lens | | | |
| 40 | Maximum Dose to Right Lens | | | |
| 41 | V5 BRIAN (Vol receiving 5 Gy to Brain) | | | |
| 42 | V6 BRIAN (Vol receiving 6 Gy to Brain) | | | |
| 43 | V10 BRIAN (Vol receiving 10 Gy to Brain) | | | |
| 44 | V20 BRIAN (Vol receiving 20 Gy to Brain) | | | |
| 45 | V40 BRIAN (Vol receiving 40 Gy to Brain) | | | |
| 46 | Volume of the brain in cc | | | |

Others:

Any other comments:

Date: Signature of the investigator

| S NO | Hosp No | Age | Gender | Diagnsis | Prescribed dose | Fractions | RIV-SCF | RIV_SCA | RIV_DCA | PTV | Tumor Vol | SCF-PTV receving 95% | receiving 95% | receiving 95% | SCF DOSE MAX | SCA DOSE MAX | DCA DOSE MAX | IN PERCENT | SCA DMA IN PERCENT |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 241905F | 33 | 2 | PA | 5400 | 30 | 17.06 | 14.52 | 16.69 | 11.24 | 4.17 | 96 | 96.9 | 97.9 | 55.03 | 54.91 | 54.96 | 101.9 | 101.7 |
| 2 | 746622F | 55 | 1 | PA | 5400 | 30 | 15.35 | 16.39 | 17.86 | 12.91 | 4.89 | 98.8 | 97.6 | 99 | 54.3 | 54.9 | 55.17 | 100.6 | 101.7 |
| 3 | 863817D | 16 | 2 | CP | 5400 | 30 | 9.43 | 9.21 | 8.93 | 6.47 | 2.04 | 96 | 96.5 | 94 | 55.28 | 54.6 | 54.79 | 102.4 | 101.6 |
| 4 | 604422D | 11 | 2 | CP | 5400 | 30 | 20.65 | 18.78 | 21.67 | 12.66 | 3.81 | 95.5 | 91 | 99.2 | 54.75 | 51.19 | 55.21 | 101.3 | 102.6 |
| 5 | 809043F | 36 | 1 | PA | 5400 | 30 | 10.76 | 10.38 | 10.52 | 7.62 | 2.53 | 95.56 | 96.2 | 92.4 | 54.64 | 55.18 | 55.4 | 101.2 | 102.2 |
| 6 | 055072G | 13 | 1 | PA | 5400 | 30 | 19.02 | 19.75 | 20.59 | 14.45 | 5.52 | 94.7 | 93.9 | 96 | 54.84 | 55.44 | 55.1 | 101.6 | 102.7 |
| 7 | 149389G | 48 | 2 | CP | 5400 | 30 | 20.16 | 16.18 | 17.16 | 13.67 | 5.02 | 99.7 | 89.5 | 93 | 55.11 | 54.98 | 55.03 | 102 | 101.8 |
| 8 | 242503G | 13 | 2 | CP | 5400 | 30 | 16.54 | 22.01 | 21.96 | 15.13 | 7.2 | 94.5 | 96.9 | 97.5 | 54.54 | 55.3 | 54.87 | 101 | 102.4 |
| 9 | 038442G | 38 | 1 | PA | 5400 | 30 | 17.06 | 17.56 | 17.19 | 14.38 | 5.68 | 97.15 | 96.7 | 95.18 | 54.6 | 55.39 | 55.38 | 101.1 | 102.6 |
| 10 | 000485G | 75 | 2 | PA | 5400 | 30 | 29.4 | 34.63 | 32.23 | 25.06 | 11.66 | 94.6 | 94.8 | 93.3 | 54.69 | 56 | 55.4 | 101.3 | 103.7 |
| 11 | 745493F | 33 | 2 | PA | 5400 | 30 | 20.63 | 20.99 | 20.84 | 16.32 | 7.83 | 95.7 | 92.7 | 91.9 | 54.88 | 55 | 54.82 | 101.6 | 101.9 |
| 12 | 246719C | 77 | 1 | PA | 5400 | 30 | 13.78 | 15.61 | 13.36 | 11.45 | 4.69 | 90 | 97.2 | 96.6 | 54.57 | 54.54 | 54.52 | 101.1 | 101 |
| 13 | 174879G | 47 | 1 | PA | 5400 | 30 | 66.65 | 57.3 | 50.72 | 41.61 | 23.62 | 95.4 | 96.6 | 96.8 | 54.95 | 55.12 | 55.12 | 101.8 | 102.1 |
| 14 | 046116G | 6 | 1 | CP | 5400 | 30 | 26.68 | 30.12 | 28.7 | 23.94 | 10.93 | 89.6 | 95.4 | 95.5 | 54.79 | 54.64 | 54.58 | 101.5 | 101.2 |
| 15 | 481775F | 28 | 2 | PA | 5400 | 30 | 34.43 | 32.62 | 27.2 | 22.02 | 9.04 | 95.9 | 95 | 98.1 | 54.69 | 54.86 | 54.78 | 101.3 | 101.6 |
| 16 | 252585G | 7 | 2 | CP | 5400 | 30 | 60.59 | 68.62 | 63.84 | 49.15 | 28.24 | 95.4 | 88 | 95.4 | 54.79 | 55.98 | 55.33 | 101.5 | 103.7 |
| 17 | 225693F | 39 | 2 | PA | 5400 | 30 | 19.18 | 19.43 | 17.83 | 14.51 | 6.63 | 97.6 | 95.7 | 98.6 | 55.15 | 56.87 | 55.47 | 102.1 | 105.3 |
| 18 | 903424C | 67 | 1 | PA | 5400 | 30 | 20.72 | 20.65 | 20.6 | 11.79 | 5.04 | 96 | 93.4 | 91.8 | 54.86 | 55.46 | 55.87 | 101.6 | 102.7 |
| 19 | 833446F | 32 | 2 | CP | 5400 | 30 | 26.96 | 27.96 | 29.36 | 23.49 | 11.53 | 95.3 | 90 | 94.5 | 55.23 | 54.97 | 55.48 | 102.3 | 101.8 |
| 20 | 177376G | 6 | 1 | CP | 5400 | 30 | 42.23 | 39.9 | 42.86 | 34.28 | 18.37 | 94.5 | 91.7 | 95.8 | 55.2 | 56.49 | 55.33 | 102.2 | 104.6 |

| DCA DMAX IN PERCENT | SCF MIN DOSE | SCA MIN DOSE | DCA MIN DOSE | SCF MIN% | SCA MIN% | DCA MIN5 | SCF MEAN DOSE | SCA MEAN DOSE | DCA MEAN DOSE | SCF MEAN DOSE IN % | SCA MEAN DOSE IN% | DCA MEAN DOSE IN % | SCF CI | SCA CI | DCA CI | HI SCF | HI SCA | HI DCA | 1 D95 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 101.8 | 48.74 | 46.09 | 49.31 | 90.3 | 85.4 | 91.3 | 53.14 | 53.12 | 53.16 | 98.4 | 93.8 | 98.4 | 1.52 | 1.29 | 1.48 | 1.07 | 1.07 | 1.07 | 51.38 |
| 102.2 | 49.25 | 46.85 | 49.48 | 91.2 | 86.8 | 91.6 | 52.72 | 53.26 | 53.47 | 97.6 | 98.6 | 99 | 1.19 | 1.27 | 1.38 | 1.06 | 1.07 | 1.07 | 51.3 |
| 101.5 | 48.68 | 44.11 | 49.05 | 90.1 | 81.7 | 90.8 | 53.25 | 53.13 | 53.03 | 98.6 | 98.4 | 98.2 | 1.46 | 1.42 | 1.38 | 1.08 | 1.06 | 1.06 | 51.01 |
| 102.2 | 43.62 | 40.99 | 49.7 | 80.8 | 75.9 | 92.1 | 53.16 | 53.37 | 53.64 | 98.4 | 98.8 | 99.3 | 1.63 | 1.48 | 1.71 | 1.06 | 1.03 | 1.08 | 51.84 |
| 102.2 | 49.7 | 40.67 | 46.61 | 92 | 75.3 | 98.59 | 52.97 | 53.04 | 53.21 | 98.1 | 98.2 | 98.5 | 1.41 | 1.36 | 1.38 | 1.06 | 1.09 | 1.08 | 51.47 |
| 102 | 48.31 | 44.2 | 48.95 | 89.5 | 81.9 | 90.7 | 53 | 53.21 | 53.36 | 98.1 | 98.5 | 98.8 | 1.32 | 1.37 | 1.42 | 1.06 | 1.09 | 1.07 | 51.71 |
| 101.9 | 48.99 | 46 | 49.12 | 90.7 | 85.3 | 91.41 | 53.32 | 52.94 | 53.88 | 98.7 | 98 | 98.3 | 1.47 | 1.18 | 1.26 | 1.06 | 1.08 | 1.07 | 51.94 |
| 101.6 | 46.12 | 46.43 | 48.35 | 85.5 | 86 | 89.5 | 52.77 | 53.52 | 53.56 | 97.7 | 99.1 | 98.8 | 1.09 | 1.45 | 1.45 | 1.07 | 1.07 | 1.06 | 51.12 |
| 102.6 | 48.67 | 46.42 | 48.42 | 90.1 | 86 | 89.7 | 52.81 | 52.87 | 53.19 | 97.8 | 95.3 | 98.5 | 1.19 | 1.22 | 1.20 | 1.06 | 1.08 | 1.08 | 51.3 |
| 102.6 | 47.51 | 45.5 | 46.32 | 88 | 84.3 | 85.88 | 52.51 | 54.04 | 53.32 | 97.2 | 100.1 | 98.7 | 1.17 | 1.38 | 1.29 | 1.07 | 1.09 | 1.08 | 51.3 |
| 101.5 | 47.1 | 47.42 | 46.89 | 87.1 | 87.8 | 86.8 | 53.02 | 53.25 | 53.07 | 98.2 | 98.6 | 98.3 | 1.26 | 1.29 | 1.28 | 1.07 | 1.08 | 1.07 | 51.3 |
| 101 | 49.08 | 49.21 | 47.34 | 90.09 | 91.1 | 87.7 | 52.3 | 53.28 | 52.73 | 97.1 | 98.7 | 97.6 | 1.20 | 1.36 | 1.17 | 1.07 | 1.05 | 1.07 | 50.89 |
| 102.1 | 44.54 | 46.36 | 47.49 | 82.5 | 85.8 | 87.9 | 53.13 | 53.31 | 52.9 | 98.4 | 98.7 | 98.1 | 1.60 | 1.38 | 1.22 | 1.07 | 1.07 | 1.08 | 51.3 |
| 101.1 | 42.7 | 47.7 | 47.57 | 79.1 | 88.3 | 88.1 | 52.71 | 53.02 | 52.97 | 97.6 | 98.2 | 98.1 | 1.11 | 1.26 | 1.20 | 1.08 | 1.08 | 1.07 | 50.76 |
| 101.4 | 48.92 | 41 | 46.83 | 90.6 | 75.9 | 86.71 | 53.05 | 53.4 | 53.13 | 98.2 | 98.7 | 98.4 | 1.56 | 1.48 | 1.24 | 1.06 | 1.07 | 1.06 | 51.59 |
| 102.5 | 47.79 | 40.49 | 45.95 | 88.5 | 75 | 85.1 | 52.79 | 53.41 | 53.12 | 97.8 | 98.9 | 98.5 | 1.23 | 1.40 | 1.30 | 1.06 | 1.11 | 1.08 | 51.84 |
| 102.7 | 49.79 | 40.3 | 49.57 | 92.2 | 74.6 | 91.8 | 53.28 | 54.17 | 53.33 | 98.7 | 100.3 | 98.8 | 1.32 | 1.34 | 1.23 | 1.06 | 1.10 | 1.08 | 51.84 |
| 103.5 | 43.96 | 45.81 | 41.2 | 81.4 | 84.8 | 76.3 | 53.13 | 53.55 | 53.68 | 98.4 | 99.2 | 99.4 | 1.76 | 1.75 | 1.75 | 1.08 | 1.08 | 1.11 | 50.89 |
| 102.7 | 47.58 | 42.57 | 47.87 | 88.1 | 78.8 | 88.7 | 53.07 | 52.98 | 53.3 | 98.03 | 98.1 | 98.7 | 1.15 | 1.19 | 1.25 | 1.08 | 1.10 | 1.09 | 51.12 |
| 102.5 | 41.41 | 30.86 | 45.97 | 77.67 | 57.17 | 85.1 | 52.97 | 53.89 | 53.37 | 98.1 | 99.8 | 98.8 | 1.23 | 1.16 | 1.25 | 1.08 | 1.12 | 1.08 | 51.3 |

| 2 D95 | 3 D95 | SCF DOSE TO LEFT EYE | SCA DOSE TO LEFT EYE | DCA DOSE TO LEFT EYE | SCF DOSE TO RIGHT EYE | SCA DOSE TO RIGHT EYE | DCA DOSE TO RIGHT EYE | SCF DOSE TO BRAIN STEM | SCA DOSE TO BRAIN STEM | DCADOSE TO BRAIN STEM | SCF DOSE TO OP CHIASM | SCA DOSE TO OP CHIASM | DCA DOSE TO OP CHIASM | DOSE TO LT OPN | SCA DOSE TO LT OPN | DCA DOSE TO LT OPN | 1 DOSE TO RT OPN | 2 DOSE TO RT OPN | 3 DOSE TO RT OPN |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 51.3 | 51.59 | 0.73 | 2.12 | 1.49 | 0.75 | 2.05 | 1.33 | 52.34 | 53.05 | 52.92 | 54.81 | 54.62 | 54.67 | 20.67 | 22.23 | 28.87 | 35.4 | 35.4 | 36.14 |
| 51.47 | 51.59 | 1.03 | 10.82 | 12.04 | 0.72 | 11.07 | 9.61 | 23.45 | 37.46 | 29.8 | 53.35 | 54.4 | 54.88 | 17.37 | 23.69 | 22.67 | 14.98 | 23.05 | 20.44 |
| 51.3 | 51.47 | 0.86 | 3.2 | 2.26 | 1.14 | 7.15 | 6.86 | 51.71 | 50.68 | 50.92 | 53.58 | 54.59 | 54.44 | 32.39 | 21.79 | 26.67 | 50.35 | 50.06 | 51.04 |
| 49.48 | 51.3 | 0.7 | 8.84 | 10.15 | 0.66 | 6.28 | 4.44 | 44.88 | 50.44 | 49 | 53.25 | 53.16 | 53.06 | 19.42 | 23.22 | 26.49 | 7.05 | 28.46 | 24.42 |
| 50.76 | 51.12 | 0.63 | 4.81 | 3.94 | 0.73 | 5.88 | 4.35 | 46.98 | 45.57 | 48.03 | 53.55 | 53.84 | 54.35 | 28.35 | 12.32 | 13.21 | 41.26 | 37.59 | 46.89 |
| 51.01 | 51.3 | 0.99 | 9.46 | 5.11 | 7.65 | 12.12 | 4.96 | 38.04 | 41.28 | 37.3 | 54.38 | 54.94 | 54.56 | 51.77 | 52.06 | 52.49 | 51.35 | 52.84 | 52.65 |
| 51.12 | 51.3 | 1.21 | 7.17 | 6.86 | 1.51 | 5.74 | 5.87 | 53.61 | 53.66 | 53.74 | 54.22 | 53.82 | 53.87 | 26.11 | 25.77 | 22.17 | 21.85 | 25.59 | 22.98 |
| 51.47 | 51.84 | 0.63 | 0.96 | 0.78 | 0.67 | 1.4 | 1.13 | 53.45 | 54.48 | 54.24 | 53.61 | 54.88 | 54.5 | 2.96 | 7.15 | 4.36 | 9.22 | 22.1 | 23.62 |
| 51.12 | 51.3 | 0.62 | 2.29 | 1.44 | 0.7 | 1.98 | 1.63 | 49.06 | 50.85 | 48.5 | 53.45 | 53.78 | 53.88 | 16.73 | 17.9 | 20.3 | 13.75 | 21.52 | 20.66 |
| 51.3 | 51.3 | 2.07 | 11.26 | 12.59 | 1.74 | 12.79 | 10.67 | 51.16 | 53.58 | 51.74 | 53.57 | 55.5 | 54.6 | 49.86 | 49.7 | 51 | 49.59 | 51.98 | 52.69 |
| 51.12 | 51.12 | 1.1 | 6.32 | 3.38 | 1.74 | 4.14 | 3.12 | 53.76 | 53.31 | 53.49 | 54.12 | 54.83 | 54.42 | 27.27 | 33.34 | 32.73 | 24.07 | 30.33 | 30.26 |
| 51.84 | 50.89 | 1.67 | 4.2 | 4.31 | 1.72 | 4.1 | 2.18 | 25.87 | 47.98 | 36.95 | 54.53 | 54.56 | 54.57 | 36.9 | 40.42 | 34.14 | 26.1 | 36 | 27.96 |
| 51.59 | 51.12 | 2.23 | 6.41 | 14.4 | 5.62 | 11.69 | 15.4 | 54.39 | 53.53 | 54.09 | 53.62 | 54.46 | 54.03 | 32.58 | 25.05 | 30.3 | 28.59 | 28.62 | 30.39 |
| 50.76 | 51.12 | 1.36 | 8.72 | 7.28 | 1.36 | 6.52 | 5.3 | 51.96 | 52.99 | 54.57 | 54 | 54.46 | 52.71 | 31 | 32.57 | 33.18 | 44.03 | 45.77 | 46.32 |
| 51.47 | 51.71 | 1.69 | 9.27 | 8.58 | 3.46 | 14.38 | 8.32 | 52.69 | 54.56 | 53.13 | 53.47 | 54.56 | 53.96 | 44.87 | 37.53 | 43.36 | 49.55 | 51.45 | 49.19 |
| 50.42 | 51.3 | 5.85 | 5.61 | 3.04 | 7.88 | 6.84 | 3.35 | 53.92 | 54.85 | 54.75 | 52.99 | 54.61 | 53.96 | 49.9 | 40.86 | 47.62 | 50.42 | 47.63 | 50.82 |
| 51.71 | 51.47 | 1.15 | 6.29 | 4.38 | 1.28 | 9.7 | 4.71 | 53.61 | 56.82 | 53.59 | 53.85 | 55.51 | 54.23 | 28.94 | 25.25 | 25.21 | 49.08 | 45.11 | 45.94 |
| 51.12 | 50.54 | 0.82 | 1.86 | 5.18 | 0.8 | 2.07 | 3.29 | 26.56 | 28.32 | 33.7 | 54.37 | 54.83 | 55.69 | 15.33 | 31.75 | 29.17 | 19.02 | 23.65 | 23.96 |
| 49.84 | 50.76 | 1.94 | 1.07 | 3.02 | 2.71 | 2.11 | 3.58 | 53.93 | 52.7 | 52.49 | 53.64 | 53.73 | 54.04 | 5.04 | 8.54 | 8.05 | 5.72 | 8.88 | 7.55 |
| 50.65 | 51.12 | 1.61 | 4.36 | 8.57 | 1.69 | 8.79 | 8.43 | 54.11 | 55.46 | 54.67 | 53.1 | 54.96 | 54.18 | 17.84 | 20.39 | 26.16 | 18.32 | 18.66 | 27.88 |

| 1 DOSE TO LT LENS | 2 DOSE TO LT LENS | 3 DOSE TO LT LENS | 1 DOSE TO RT LENS | 2 DOSE TO RT LENS | 3 DOSE TO LT LENS | 1 V5 BRIAN | 2 V5 BRAIN | 3 V5 BRAIN | 1 V6 BRAIN | 2 V6 BRAIN | 3 V6 BRAIN | 1 V10 BRAIN | 2 V10 BRAIN | 3 V10 BRAIN | 1 V20 BRAIN | 2 V20 BRAIN | 3 V20 BRAIN | 1 V40 BRAIN` | 2 V40 BRAIN | 3 V40 BRAIN | SCF QOC SCF | SCA QOC SCA | DCAQOC DCA |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 0.35 | 0.42 | 0.39 | 0.32 | 0.42 | 0.39 | 270 | 342 | 339 | 261 | 272 | 272 | 234 | 163 | 164 | 85 | 68 | 74 | 24 | 22 | 23 | 95.05 | 89.89 | 96.11 |
| 0.38 | 8.01 | 9.02 | 0.35 | 7.03 | 5.34 | 410 | 506 | 525 | 397 | 372 | 385 | 346 | 189 | 193 | 66 | 75 | 68 | 25 | 28 | 68 | 96.00 | 91.37 | 96.42 |
| 0.34 | 0.34 | 0.35 | 0.36 | 0.54 | 0.35 | 293 | 308 | 297 | 283 | 279 | 272 | 245 | 153 | 163 | 40 | 44 | 50 | 14 | 13 | 14 | 94.84 | 86.00 | 95.58 |
| 0.3 | 5.06 | 6.48 | 0.33 | 2.14 | 1.81 | 381 | 526 | 543 | 367 | 421 | 424 | 256 | 228 | 241 | 119 | 85 | 88 | 51 | 38 | 38 | 85.05 | 79.89 | 96.95 |
| 0.28 | 1.08 | 0.59 | 0.32 | 1.19 | 0.48 | 343 | 379 | 433 | 323 | 257 | 301 | 171 | 111 | 114 | 117 | 40 | 43 | 19 | 17 | 17 | 96.84 | 79.26 | 103.78 |
| 0.45 | 4.63 | 2.5 | 0.67 | 5 | 2.07 | 446 | 552 | 418 | 435 | 441 | 381 | 389 | 221 | 215 | 76 | 74 | 104 | 29 | 29 | 33 | 94.21 | 86.21 | 95.47 |
| 0.34 | 0.51 | 0.5 | 0.34 | 0.47 | 0.42 | 342 | 516 | 517 | 331 | 429 | 426 | 296 | 238 | 239 | 98 | 79 | 80 | 35 | 31 | 30 | 95.47 | 89.79 | 96.22 |
| 0.31 | 0.42 | 0.35 | 0.34 | 0.45 | 0.42 | 389 | 484 | 444 | 369 | 448 | 375 | 270 | 275 | 244 | 175 | 135 | 138 | 33 | 35 | 44 | 90.00 | 90.53 | 94.21 |
| 0.3 | 1.21 | 0.51 | 0.33 | 1.09 | 0.38 | 410 | 544 | 610 | 398 | 434 | 458 | 355 | 194 | 196 | 82 | 87 | 72 | 25 | 28 | 26 | 94.84 | 90.53 | 94.42 |
| 0.76 | 7.29 | 7.05 | 0.56 | 8.05 | 2.98 | 446 | 752 | 493 | 434 | 661 | 411 | 369 | 324 | 239 | 110 | 110 | 116 | 43 | 44 | 46 | 92.63 | 88.74 | 90.40 |
| 0.53 | 1.36 | 1.19 | 0.56 | 0.64 | 1.38 | 471 | 576 | 531 | 458 | 445 | 437 | 413 | 187 | 191 | 81 | 74 | 79 | 28 | 27 | 28 | 91.68 | 92.42 | 91.37 |
| 0.36 | 2.17 | 0.96 | 0.51 | 2.11 | 0.55 | 326 | 447 | 514 | 317 | 401 | 414 | 285 | 242 | 183 | 73 | 57 | 47 | 19 | 16 | 16 | 94.83 | 95.89 | 92.32 |
| 0.95 | 1.94 | 4.75 | 0.97 | 5.45 | 5.21 | 582 | 1067 | 1025 | 569 | 949 | 921 | 531 | 492 | 512 | 304 | 203 | 181 | 105 | 86 | 81 | 86.84 | 90.32 | 92.53 |
| 0.54 | 3.14 | 1.63 | 0.56 | 2.83 | 1.51 | 595 | 623 | 588 | 576 | 507 | 459 | 496 | 295 | 295 | 131 | 154 | 152 | 50 | 54 | 53 | 83.26 | 92.95 | 92.74 |
| 0.61 | 5.82 | 3.13 | 0.73 | 8.56 | 3.58 | 456 | 692 | 672 | 444 | 533 | 556 | 414 | 252 | 252 | 102 | 110 | 90 | 40 | 42 | 38 | 95.37 | 79.89 | 91.27 |
| 1.31 | 0.85 | 0.9 | 1.3 | 0.87 | 1.05 | 714 | 813 | 764 | 699 | 757 | 714 | 632 | 604 | 562 | 424 | 337 | 329 | 109 | 120 | 123 | 93.16 | 78.95 | 89.58 |
| 0.48 | 1.02 | 2.51 | 0.48 | 2.25 | 2.04 | 313 | 262 | 560 | 305 | 250 | 451 | 285 | 190 | 186 | 86 | 84 | 58 | 21 | 21 | 22 | 97.05 | 78.53 | 96.63 |
| 0.29 | 0.74 | 3.13 | 0.33 | 0.9 | 1.37 | 347 | 586 | 613 | 337 | 448 | 523 | 310 | 234 | 289 | 136 | 104 | 119 | 32 | 30 | 29 | 85.68 | 89.26 | 80.32 |
| 0.68 | 0.51 | 0.46 | 0.64 | 0.57 | 0.47 | 539 | 717 | 676 | 523 | 638 | 609 | 462 | 360 | 392 | 199 | 154 | 152 | 54 | 52 | 50 | 92.74 | 82.95 | 93.37 |
| 0.9 | 1.26 | 3.36 | 0.93 | 0.96 | 1.98 | 590 | 701 | 806 | 573 | 640 | 738 | 520 | 433 | 488 | 363 | 237 | 226 | 76 | 63 | 74 | 81.76 | 60.18 | 89.58 |